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The Unintended Deadlock: How Industry and Regulators Are Stranding Global Patients

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Executive Summary

The pharmaceutical landscape could enter a state of terminal fracture as U.S. and EU regulatory reforms collide at full force. The U.S. "Regulatory Trinity" (GENEROUS, GLOBE, and GUARD) establishes international price referencing that penalizes global price transparency, while the EU's new "access conditionality" attempts to incentivize launches in all member states. This collision creates an "unintended deadlock", forcing manufacturers to bypass or postpone European markets to protect U.S. revenue. Simultaneously, the "Pill Penalty" and "Orphan Distortion" drive innovation toward complex biologics and niche patient segments, creating a physical and diagnostic infrastructure barrier that effectively isolates patients in Europe and Low- and Middle-Income Countries (LMICs) from innovation.

1. The Transatlantic Regulatory Collision

Following our previous analysis on why investors will push for a wave of geographic corporate spin-offs, it has become increasingly clear that the resulting "decoupling" is not just a financial strategy—it is a brewing patient access crisis.1 While the initial analysis focused on the structural breakdown of the global pharma model, this paper investigates the human cost for patients and their families in Europe and Low- and Middle-Income Countries (LMICs).

We are currently witnessing a **regulatory collision**: European and U.S. policymakers appear to have designed their respective reforms in isolation, with the EU pharmaceutical package giving limited consideration to the international pricing environment now being reshaped by the U.S. One Big Beautiful Bill Act (OBBBA).2 The result is a deadlock where well-intentioned access mandates in Europe are neutralized by the gravitational pull of U.S. price referencing.

2. The Mechanics of Global Access Fragmentation

A. The Launch Sequence Trap: Europe's Regulatory Blind Spot

The most immediate impact of U.S. reform on global patients is a strategic shift that traps European patients in an unintended deadlock between the U.S. "Regulatory Trinity" (GENEROUS, GLOBE, and GUARD models) and the EU's Pharma Package with the new "access conditionality".[3, 4]

The Pincer Effect

- **The EU Mandate:** To secure full regulatory data protection (RDP), the EU now requires that manufacturers launch in all 27 Member States within three years.[5]
- **The U.S. Anchor:** Simultaneously, the U.S. models now use reference prices from some of those same European countries—specifically including traditionally lower price EU states—as a mandatory benchmark to set U.S. Medicaid and Medicare prices.[6, 4]

Unless EU member states radically reverse their price control policies, this forces manufacturers into an impossible choice: satisfy the EU launch mandate and trigger massive rebate liabilities in the U.S. or **initially bypass the European market entirely** to protect the U.S. revenue anchor. When protecting U.S. prices is considered more important, even patients in high-income European markets will be cut off from therapeutic innovation or at least face significant delays in availability and access.

This regulatory deadlock is not a theoretical economic problem; it is a clinical one. Historical data on oncology access already documented the devastating impact of access delays: Across Europe, delayed access to oncology drugs has potentially resulted in the loss of **more than 30,000 life years.**[7]

B. The Infrastructure Barrier: How the "Pill Penalty" Abandons Patients in LMICs

The "Pill Penalty"—a provision where small-molecule oral drugs are eligible for CMS price negotiation after only 7 years (effective at year 9) while biologics receive 11 years (effective at year 13)—is driving R&D away from the very treatments most viable for the majority of patients worldwide.[8] In a U.S.-centric business model, some oral programs are no longer considered viable. Where there is a valid alternative that falls under the FDA's Biologics License Applications (BLA) process, it will be prioritized because of the longer exemption from price negotiations.

From Oral Ease to Biologics Complexity

More important than the number of drugs being developed and approved is *what kind* of drugs the industry is being incentivized to develop:

- **The Loss of the "Shelf-Stable" Cure:** Small molecules (pills) are the backbone of global health because they are typically thermostable and can reach even remote areas without advanced logistics. For U.S.-centric companies, the deck has been stacked in favor of biologics, antibody drug conjugates, and cell therapies, potentially accelerating the shift away from small molecule development observed over the past decade.[9]

- **The Distribution Chasm:** These drugs typically require complex manufacturing and a robust "2–8°C cold chain" distribution and often specialized clinical staff for administration.[10] In the 113 countries covered by the Access to Medicine Index, innovation in the form of a biologic instead of a pill often means a life-saving therapy becomes physically unreachable due to unstable power grids and lack of infusion centers.[11]
- **The Chronic Disease Gap:** With biologics often developed for indications such as oncology and immunology, R&D could shift further away from widespread diseases such as diabetes and hypertension, leaving a large share of patients stranded with today's therapeutic status quo.[12]

C. The Orphan Distortion: Sidelining Common Conditions

The OBBBA expanded the Orphan Drug Exclusion, allowing products with multiple orphan designations to remain exempt from price negotiation as long as all approved indications are for rare diseases.[13] This creates a powerful incentive for manufacturers to prioritize orphan indications within a development program or to micro-segment patient populations using advanced biomarkers, genetic testing, or state-of-the-art imaging techniques to maintain orphan status for as long as possible.

While improved incentives to develop treatments for rare diseases can benefit certain patient groups, this strategy can also create a new form of "neglected diseases":

- **Incentivizing Complexity over Scale:** By rewarding manufacturers for keeping patient groups small and genetically defined, U.S. law incentivizes the delay of drug development in broader, less-stratified populations. Therefore, patients with more common diseases will have to wait longer for new treatment options.
- **Advanced Diagnostics as an Access Filter:** Innovation is increasingly "tied" to expensive diagnostics such as molecular testing, Next-Generation Sequencing (NGS), or PET scans that are not widely available in many regions. In Europe, for example, **less than 10% of specimens requiring molecular testing are currently analyzed with NGS**.[14] If a healthcare system does not provide or reimburse the necessary testing, the drug is effectively unavailable even if technically "approved". [15]
- **Limiting the Evidence Base:** Smaller target populations mean smaller clinical trials, making it less likely that rare but potentially important safety signals are detected during development.

3. Recommendations for International Healthcare Systems

Policy makers cannot wait and hope for U.S. regulation to change or for legal challenges against the TrumpRx platform to succeed. Strategic shifts in R&D priorities will happen mostly in silence and take years to impact clinical practice. Development programs not initiated are not discussed in SEC filings or investor calls, creating a massive "invisible pipeline" of lost opportunities. Patients will never know they might have had the chance for a new and better treatment option simply because the research was abandoned years before a trial could even begin.

To ensure their patients are not left behind in the global innovation cycle, international health systems must act today. They need to rethink their approach to market participation and how to incentivize the development of the treatments they need.

A. Fostering Alternative Innovation Hubs

When traditional biopharma companies become even more U.S.-centric or are pressured by investors to separate into independent U.S. and International companies as previously predicted, health systems must look to alternative global sources for innovative therapies and treatment modalities that meet the needs of their patients.

While the international spin-offs might aim to fill this void, we believe that this disruption will fuel the global expansion of companies from other regions, especially China and India. The ongoing growth of drug discovery in these countries and their experience in developing drugs specifically for LMICs will put them in the prime position to provide a necessary competitive counterweight to the U.S.-centric R&D model.[16]

Policy makers in Western countries will need to rethink how they can create an economic and regulatory environment that enables the international spin-offs to successfully innovate and compete with their emerging competitors. Otherwise, regulators in developed countries will soon face the choice of either adapting their standards to welcome these new players that promise patients access to innovative treatment options at potentially lower costs or risk their patients being cut-off from innovation from both the U.S. and emerging innovators.

B. Recognition of Broader Societal Value

Healthcare systems should move beyond narrow clinical endpoints and account for societal benefits of new treatment options, including caregiver impact and productivity gains.[4] Recognizing the true value of innovation strengthens the case for investment in healthcare infrastructure, advanced diagnostics and new treatment options. But the harsh reality is that this requires more than a change in regulation or HTA methodology – it requires prioritization of healthcare spending over other budget items as in the US-UK Economic Prosperity Deal. [17]

C. Creating a truly Single Market in Healthcare

The member states of the EU must decide if they can afford continued fragmentation into a multitude of national and regional healthcare systems. A single market for healthcare could better signal the region's preferences, reward innovation, and create more predictable demand as a counterweight to the U.S. or Chinese markets that will otherwise dominate pharma's business strategy.

Conclusion

The "Unintended Deadlock" is a structural byproduct of uncoordinated global regulation. As the U.S. market actively references the world, and the world attempts to force access through mandate, patients are caught in the middle. Sovereignty in 2026 will be defined by a healthcare system's ability to bridge

the "Access Chasm" through its own innovation hubs, diagnostic infrastructure, and a modernized recognition of societal value.

DR. SCHAUFLER ACCESS ADVISORY can help you navigating the complexity of the global policy and regulatory landscape to achieve sustainable patient access. To learn more about how we can support you visit https://www.dr-schaufler.com.

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