Biosimilar Substitution

A Collaborative Approach to Pharmacovigilance

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Background

- **Responsible use of biologic and biosimilar medicines is complicated**
  - Efficacy/effectiveness gap
  - Safety/preventable adverse drug events
  - Innovation/affordability conflicts
- **Medication-use is a team effort**
  - The greatest value from an investment in pharmacotherapy results from collaboration among health care professionals and patients
- **Accountability**
  - Health care professionals -> their patient (Regulated by the States)
  - Pharma -> innovations for patients (Regulated by the Federal Gov't)
  - Insurance companies/PBMs -> Saving money (Regulated???)

Benefits of Biosimilar Medicines

Increased treatment choices:

- Patients with conditions treated by biologics often struggle for years, trying multiple products, before becoming stable.

Cost savings:

- Unlike generics, which save 40-80%, due to higher development costs biosimilars are expected to save payers 15-30%.[1]
- A 2014 RAND Corporation study estimated 10-35% cost reduction in U.S. [2] This has been borne out in a 2018 RAND study.[3]
- COMPETITION IS KEY: In Europe, savings of 35%--70% have been seen.[4] : "the available data in Europe show that health systems are achieving discounts of as much as 70% for some drugs, **primarily for molecules that have 3 biosimilar products available."**

1 Generics and Biosimilars Initiative Journal (GaBI Journal). 2012;1(3-4).120-6. DOI: 10.5639/gabij.2012.0103-4.036
2 https://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE127/RAND_PE127.pdf
3 http://www.fiercepharma.com/story/merck-discounts-remicade-uk-it-tries-fend-biosimilars/2015-10-26

Issues Surrounding Biosimilar Substitution

- Under what circumstances may a pharmacist substitute a biosimilar (approved by FDA as interchangeable) without the involvement of the physician
- What communication is required between pharmacist and:
  - Physician
  - Patient
- What records must be kept of the substitution?
- This is the purview of state government: Legislatures, Boards of Pharmacy

Why are these Concerns Important?

- Patient always needs to be informed about the medicine he/she is receiving in order to make informed choices and be an **effective partner in care**.
- Physician needs to be **aware of what medicine patient is receiving** to provide proper care.
- **Accurate patient record** must be kept for pharmacovigilance/post-market monitoring for adverse events and efficacy
- Physicians and pharmacists have a **responsibility to the patient and to the larger community** (other healthcare providers, regulators, manufacturers) to work collaboratively together – that includes **clear, timely communication.**

So How Do Advanced Countries Deal With Automatic Substitution of Biosimilars?

EU and Canada: Oppose Automatic Substitution But Leave to Provinces/Member States

- The EMA advises that: "the physician should be in charge of the decision to switch between the reference and biosimilar, or vice versa."[1]
- "Health Canada does not support automatic substitution of a Subsequent Entry Biologic for its reference biologic drug and recommends that physicians make only well-informed decisions regarding therapeutic interchange".[2]

1 European Medicines Agency. Questions and Answers on Biosimilar Medicines (Similar Biological Medicinal Products). London: European Medicines Agency; 2012. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2009/12/WC500020062.pdf. Accessed November 6, 2012.

2 http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/seb-pbu/01-2010-seb-pbu-qa-qr-eng.php

2 Canadian Provinces (British Columbia and Alberta) have begun or are about to begin mass forced-switching of 50,000+ patients on biologics.

- Patients will be switched from their current biologic to the government-chosen biosimilar.
- Proponents, including British Columbia Health Minister Adrian Dix, cited Europe's much higher rates of biosimilar usage (and savings) as a reason to adopt the policy.
- He cited B.C.'s biosimilar uptake rate as around 8%.
- By contrast, some European countries have much higher biosimilar uptake rates. These can be as high as 91% for older, simpler biosimilars, and as high as 43% market share for newer, more complex products, (post-2013), such as monoclonal antibodies.
- **However, as we will see, substitution policies in Europe which led to these rates are very different from those being advanced in Canadian provinces.**

GaBI Journal Whitepaper: The "European Blueprint"

"**Several key conditions** to achieve sustainable biosimilar markets can be identified and may be considered as **'must haves' for the long-term success of these markets."**

(1) Physicians should have the **freedom to choose** between off-patent originator biologics and available biosimilars.

(2) Tenders should include multiple value-based criteria beyond price (e.g. education, services, available dose strengths) and provide **sufficient broad choice** (multi-winner tenders vs. single-winner tenders) to ensure continuity of patient supply and healthy competition.

(3) A **level playing field** between all participating manufacturers is the best way to foster competition; mandatory discounts which place artificial downward pressure on manufacturers do not offer a sustainable market environment.

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GaBi GENERICS AND BIOSIMILARS INITIATIVE

Building trust in cost-effective treatments

Western Europe: Automatic Substitution is RARE.

- In the vast majority of European countries, the payer continues to reimburse for multiple products.
- This ensures a **robust and sustainable biosimilar market with multiple suppliers in a given product class.**
- Even in Norway with a national tendering system, physicians retain the prescription choice among all available products but are strongly encouraged to choose the lowest priced product for new (naive) patients.
- Only Denmark, following a transparent national tender process, will solely reimburse the winning product, except in rare substantiated circumstances.
- **No European country has stopped reimbursement of an originator product through an arbitrary government fiat.**

Automatic Substitution in Eastern Europe: Permitted

ESTONIA: Permitted. Patient can refuse and pay price difference out-of-pocket.

LATVIA: Non bio-naïve patients can refuse and pay cost difference; the physician can prevent substitution. Others must use cheapest product.

POLAND: Permitted, pharmacists are to discuss with patient.

RUSSIA: Physicians prescribe by INN, substitution is permitted, but the physician can prevent substitution for a medical reason. Patients can buy brand name out-of-pocket.

Automatic Substitution Policy Around the World

AUSTRALIA: Permits automatic substitution (“a-flagging”) of biosimilars, physicians can prevent substitution by writing “Dispense As Written.”

LATIN AMERICA: A range of policies. Where protections exist for physician prescriptive autonomy, enforcement is not consistent.

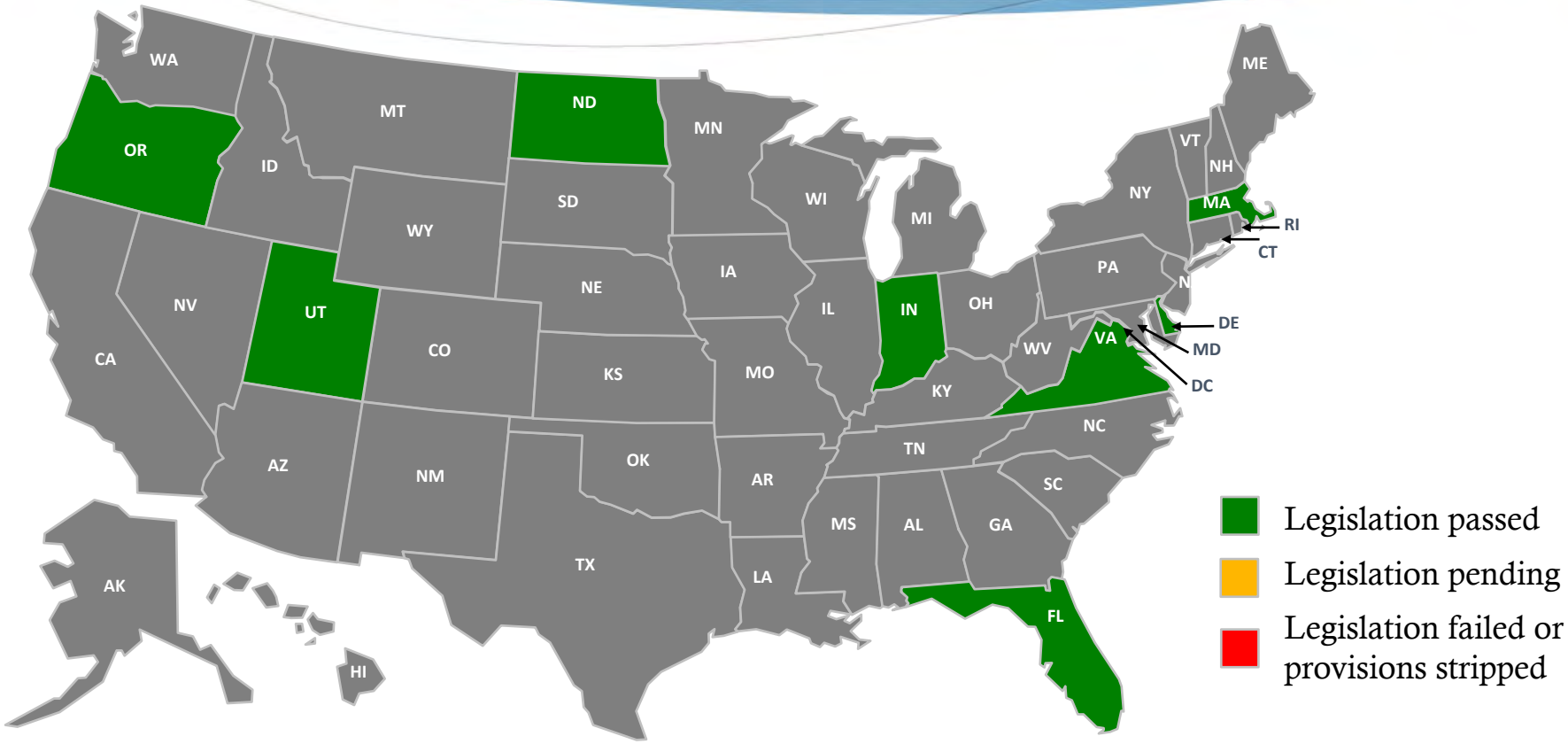
Biosimilar Substitution Policy in the U.S.

- US: 46 states permit automatic substitution **of "interchangeable" biosimilars.**
- In these states, physicians can prevent substitution and are to be communicated which product was dispensed.
- FDA silent on pharmacy substitution of non-interchangeable biosimilars.
- Private payers (PBMs) decide which product is on formulary - the originator or a biosimilar.

Common Features of U.S. State Substitution Laws

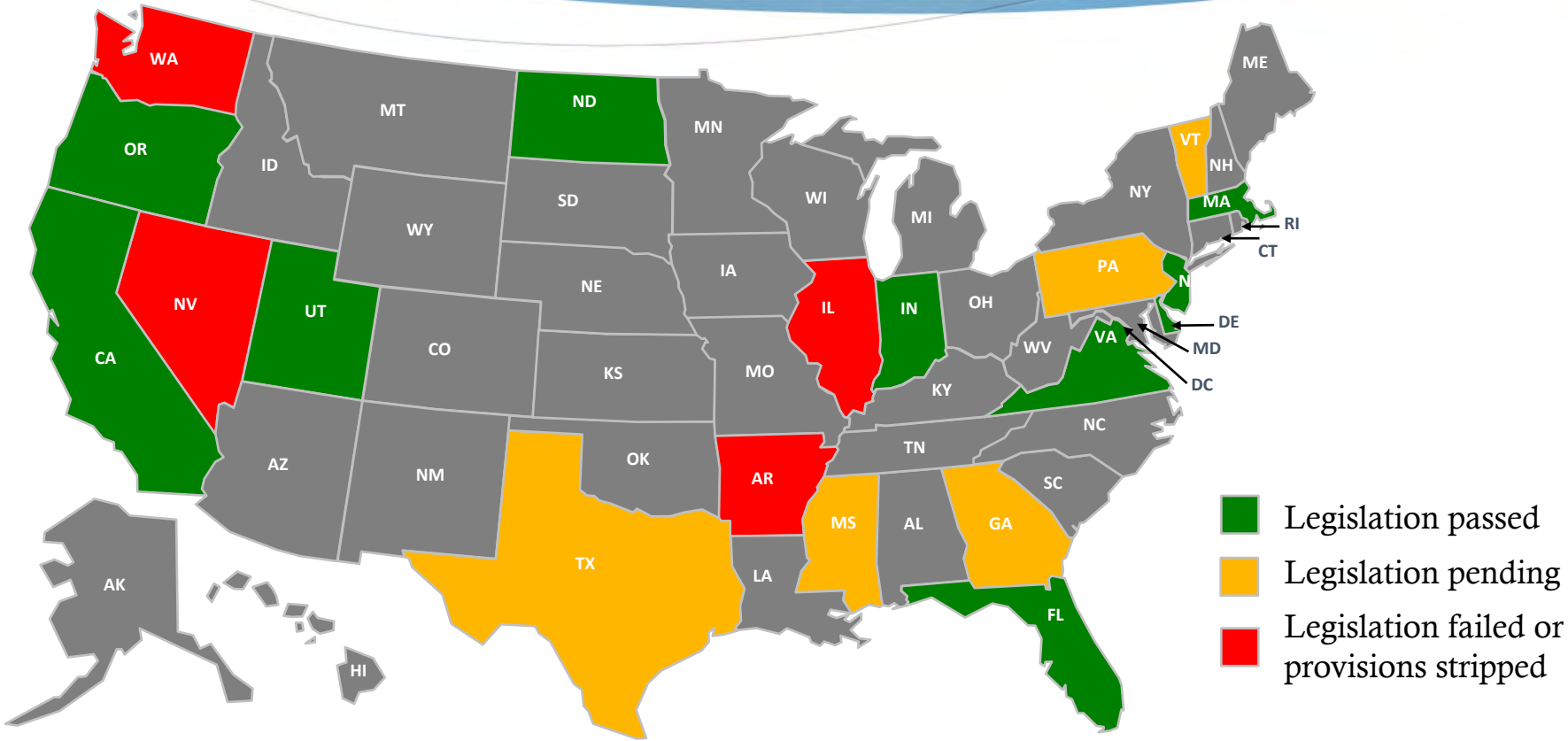
- Permits only substitution of "interchangeable" biosimilars.
- Require pharmacist to communicate which product – biosimilar or reference- was dispensed to patient within 3-5 business days.
- Allow physician to specify "do not substitute" or similar directive.
- Pharmacist to keep records for 2 years.

2014: Communication Requirements by State



Rev. 11/15

2015: Communication Requirements by State



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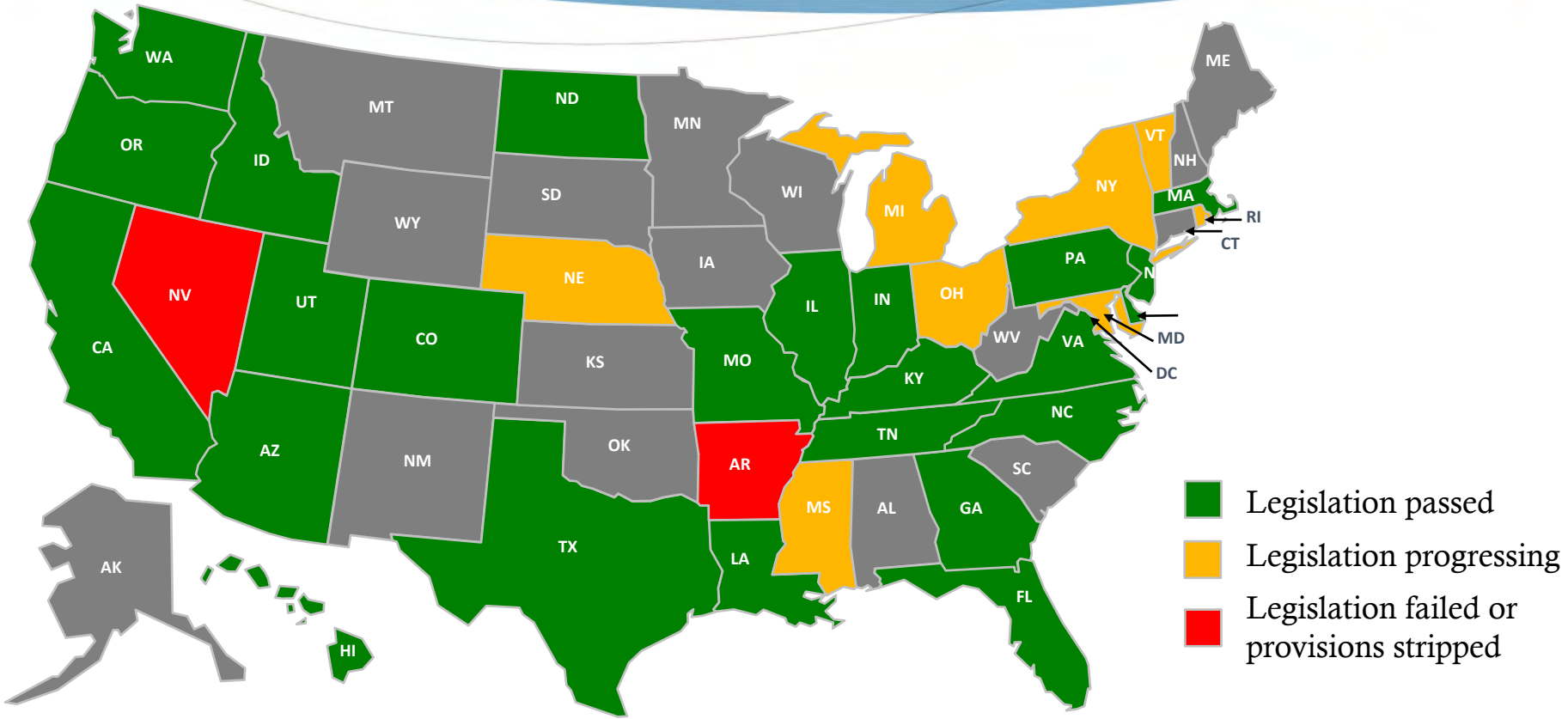
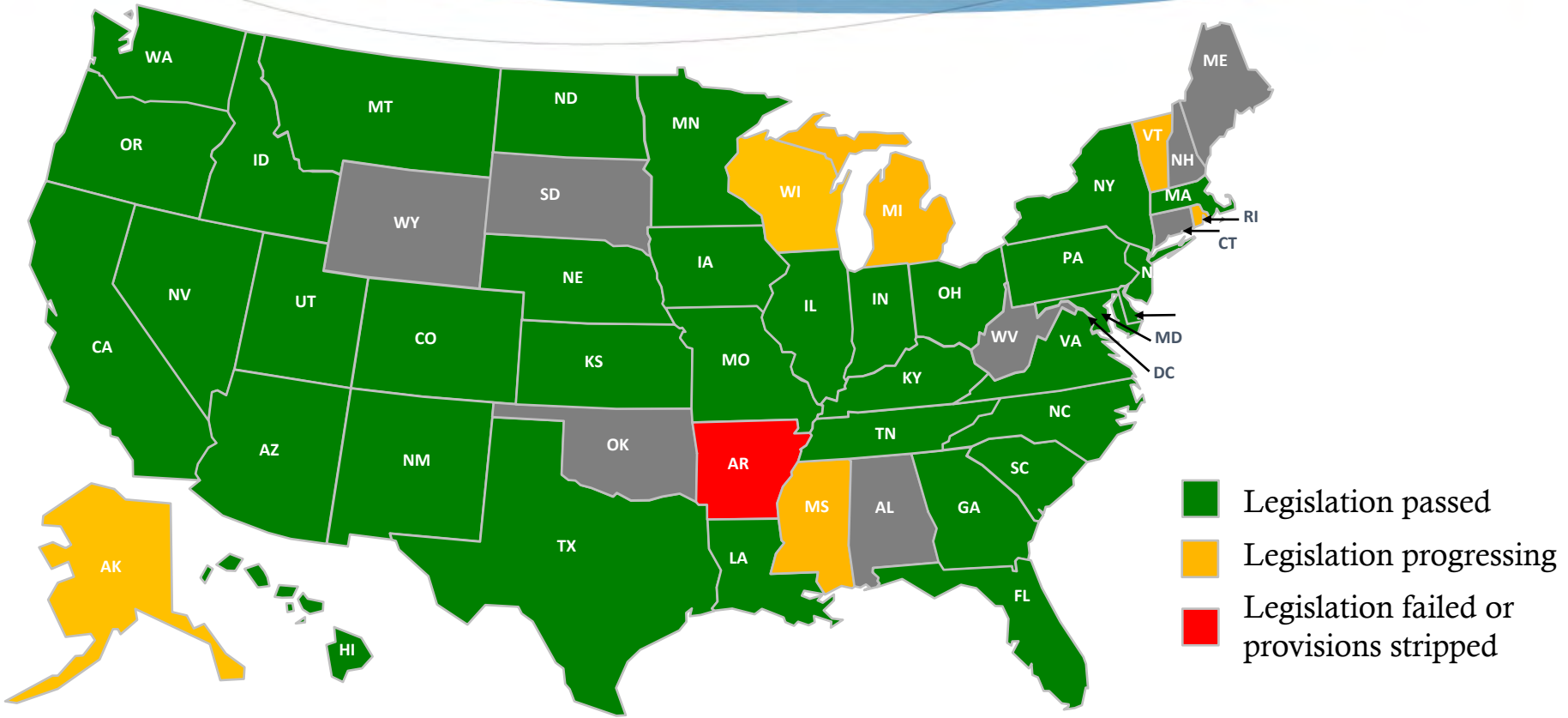
2016: Communication Requirements by State



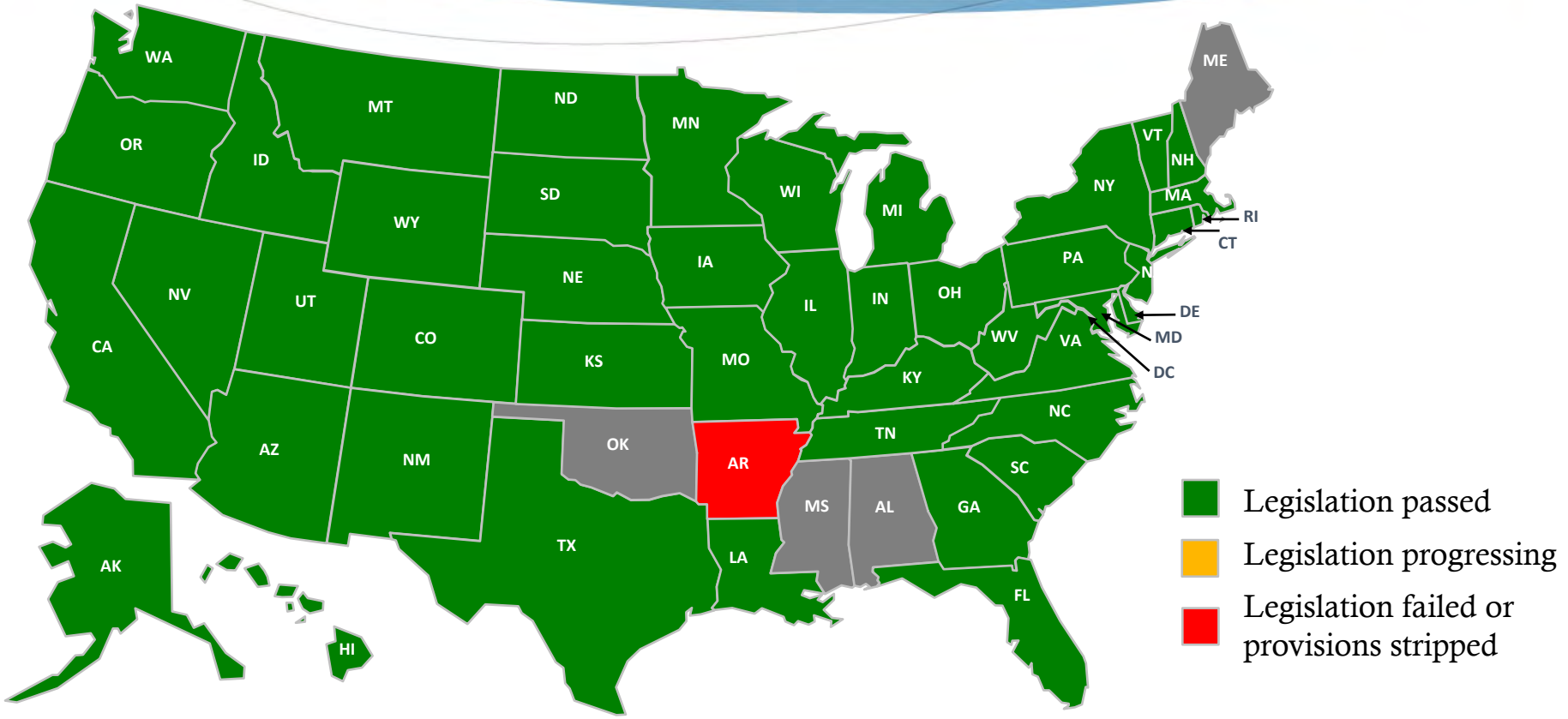
Rev. 09/14/16

2017: Communication Requirements by State



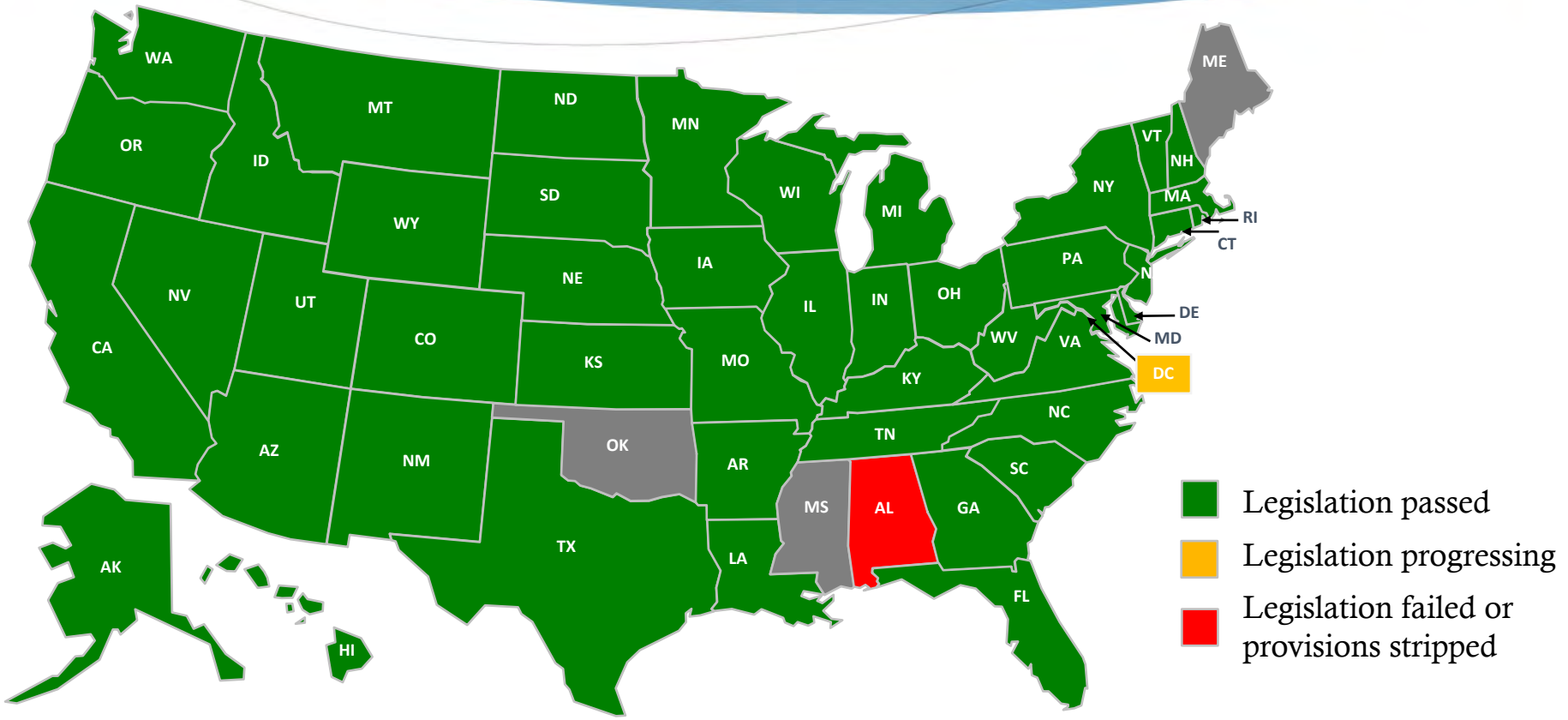
Rev. 12/17

2018: Communication Requirements by State



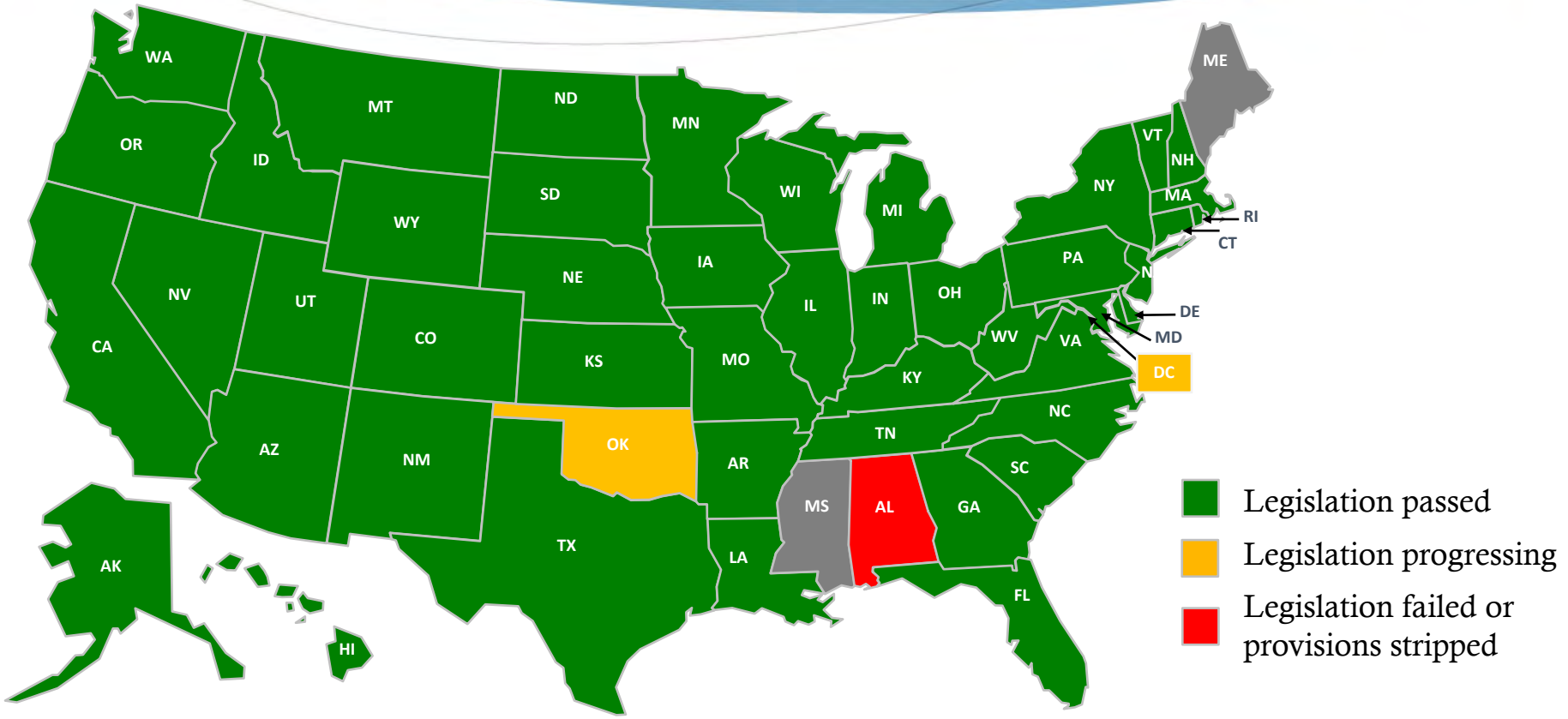
Rev. 09/11/18

2019: Communication Requirements by State



Rev. 02/16/20

2020: Communication Requirements by State



Rev. 02/16/20

Comparison Between Laws in Tri-State Area

State	Bill Signed	FDA Must Certify Interchan-geability	Prescriber Communication	Patient Notification	Prescriber's "Brand Medically Necessary" Blocks Substitution	Pharmacy Records Must Be Retained	Posted List of Interchan-geables
New York	S 4788 of 2017 Signed 10/23/17	Yes	5 days	N/A	Yes	No	Yes
Connecticut	SB 197; signed 2018;	Yes	3 days	Yes	Yes	Yes 3 years	No
New Jersey	A 2477; signed 11/9/2015;	Yes	5 days	N/A/	Yes	Yes same as Rx	Yes

Early Criticisms of U.S. Substitution Legislation

- Legislation premature? There are NO biosimilars in the United States marketplace.
- Premature laws create confusing patchwork of state substitution laws.
- Could legislation undermine public confidence in biosimilar medicines?

- First biosimilar approved March 6, 2015. Now 26 approved, about half on market, and PBMs are switching patients.
- Pharmacists, physicians need to work together to educate lawmakers in remaining states, extend a common standard for these laws.
- To the contrary, Physicians defaulting to "do not substitute" as only means of knowing what patient is receiving would undermine biosimilar adoption.

Initial Resistance from Pharmacists

- Many **state pharmacy societies** had concerns that the word "notify" implied they were subservient to physicians, and preferred the word "communicate", which implies collaboration.
- **Pharmacies** also considered the initial timeframe allotted for notification, and the length of the record-keeping provisions to be onerous.
- While helping patients and physicians, bills also **empower pharmacists** to offer lower-cost alternatives to patients without seeking authorization from physicians.
- Yet as they were made aware of the benefits the communication provisions offer to patients, they have dropped their opposition and the legislation passed.

Today automatic substitution **faded as an issue of debate** among the two national pharmacy societies, ASHP and APhA.

Physician/Pharmacist Collaboration is Key

- Physicians have the authority to specify **"do not substitute"** for biological products and that specification overrides any policy – e.g. by payers or state law – that would have substitution be the standard or default practice.

- Physicians and pharmacists should **work collaboratively** to ensure that the treating physician is aware of the exact biologic – by manufacturer – given to a patient in order to facilitate patient care and accurate attribution of any adverse events that may occurs.

Common Ground Between Physicians and Pharmacists

- Both healthcare providers, who share concern for our patients
- Both experienced with and knowledgeable about medications
- Both incentivized to perform good pharmacovigilance
- Both want a good track-and-trace system for adverse events
- Both support good record keeping.

Collaboration among Pharmacists, Physicians, Manufacturers on substitution bills has resulted in improved legislation

2013 Bill Language		2016-Present Bill Language
"Notification"	→	**"Communication"**
Notification **only if biosimilar substituted**	→	Communication of which biologic was was dispensed- **innovator / biosimilar**
72 hours to notify	→	**5 days** to communicate
Must retain records for **5 years**	→	Must retain records for **2 years**

Timing of Communication

- The timing of the communication process must not impose an undue burden on the pharmacist.
- Communication of a substitution is after dispensing.
- Must be timely enough to facilitate **accurate record keeping** and **attribution of adverse events** by the physician.

Medication-use system

- Prescribing
- Preparation
- Dispensing
- Administration
- Monitoring

Strategies for Improving Prescribing

- Collaborative practice that includes a pharmacist
- The formulary system
- Therapeutic interchange (NOT substitution)
- Evidence-based clinical practice guidelines
- Clinical decision support systems
- Metrics and performance management
  - Effectiveness
  - Safety
  - Cost

Added Value of Pharmacists

- Prudent purchasing
- Inventory control
- Managing waste
- Managing utilization
- “Balanced scorecard” (pharmacoeconomics)
- Proactive awareness

Conclusions

- The pharmacist's responsibility does not end with the patient.
- As with vaccinations, it is a matter of responsibility to a larger community.
- Pharmacists have a larger responsibility to work collaboratively with physicians, regulators, manufacturers and others to create a strong pharmacovigilance system to protect everyone.
- Clear communication between all parties is essential for the successful rollout of biosimilars- not only in their naming and when they are substituted.
- As clinicians, pharmacists also play a key role as a learned intermediary, balancing patient-specific factors against the population-derived factors considered by payers (government, private insurers).

Thank You
For Your Attention