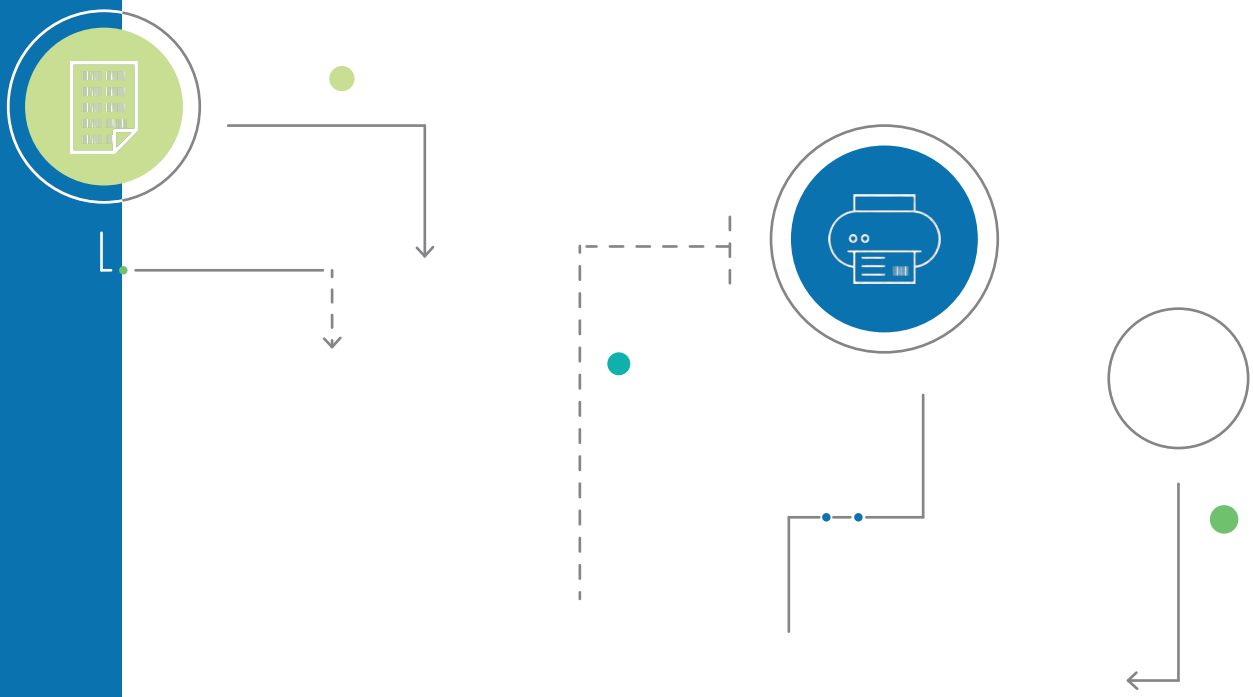

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Achieve Compliance: Converting U.S. Prescribing Information (USPI) Labels

How can the new labeling rules cause pharmaceutical companies to pull their product off the shelf or halt the drug development process?

NUMBER ONE

Physician Labeling Rule (PLR)

The Physician Labeling Rule (PLR) requires prescription drug labeling to be formatted into three sections with the intention to make information easier to read and to provide health care professionals with clear and concise prescribing information. Labels now include a *"Highlights of Prescribing Information"* section containing bulleted information, an annotated *"Table of Contents"* section, and a *"Full Prescribing Information"* section containing detailed information required for safe and effective use of the prescription drug product. Other useful information includes Boxed Warnings (in bold font), recent major changes, and patient counseling instructions.

According to a prescription information labeling analysis conducted by the FDA in November 2019, only 65% of New Drug Applications (NDAs) and 44% of the Abbreviated New Drug Applications (ANDAs) are in PLR format. This format is highly encouraged to be used for submission purposes by the FDA because it allows for clear and up-to-date communication surrounding the drug. Additionally, the rule enforces better management of the risks of medication use and reduction of medical errors, such as dose miscalculation. It also makes prescription information more accessible for use with electronic prescribing tools and other electronic information resources like DailyMed.

Specifically, the Food, Drug and Cosmetics Act mandates the FDA to require all NDAs, Biologics Licensing Applications (BLAs), and Efficacy Supplements submitted for approval on or after June 30, 2006, to conform to the PLR rule [21 CFR 201.56 (c)(1)]. In addition, all NDAs, BLAs, and Efficacy Supplements approved on or after June 30, 2001 must be converted to the PLR format, as per the labeling implementation schedule stated in the regulations [21 CFR 201.56 (c)(2)(3)(4)(5)(6)]. While the PLR format is strongly encouraged, in 2019 it was reported that only 234 voluntary conversions were approved. However, the PLR only applies to products approved under an NDA, BLA or Efficacy Supplement ES from 30 June 2001 to 30 June 2006, as well as all products thereafter.

NUMBER TWO

Pregnancy Lactation Labeling Rule (PLLR) Conversions

The new *Pregnancy Lactation Labeling Rule* (PLLR) in the U.S. Prescribing Information (USPI) was established to help benefit pregnant women, nursing mothers, and their children by changing the content and format of the information presented in prescription drug labeling in the PLR. Manufacturers must incorporate detailed information on pregnancy and lactation risk summaries (human & animal data), pregnancy exposure registries (if applicable), PK/PD data, pharmacovigilance data, pregnancy testing, contraception and infertility (if applicable).

The recent changes to the FDA drug labeling for pregnant and lactating women will make prescribing decisions easier and the information will be far more complete, current and in compliance with the PLLR.

· In contrast to the old system, where prescribers use letter categories — **A, B, C, D, and X** — to evaluate safety precautions, the PLLR helps prescribers assess the benefits and risks of medication for pregnant and lactating women in a comprehensive manner by providing risk summaries.

· All new NDAs, BLAs and Efficacy Supplements submitted on or after 30 June 2015 are required to submit the labeling compliant with the PLLR.

According to the FDA's tracking of PLLR conversion labeling in 2019, only 335 out of 620 applications submitted were compliant with the new PLLR format.

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NUMBER THREE

Trouble Converting Current USPI to New PLR and PLLR Formats? Consider it Done!

To meet regulatory labeling requirements, FlexPro's team of elite subject matter experts provide support in converting old format labeling into the new PLR and PLLR formats.

Regulatory support related to label submissions include:

- Support for strategy and preparation, including:
  - Initial submission
  - Amendments
  - Associated change control activities
  - Compliance initiatives
- Draft and review of clinical and post-market labeling, including:
  - U.S. Prescribing Information (USPI)
  - U.S. Medication Guide (MedGuide)
  - Patient Package Insert (PPI)
- Subject Matter Expert consulting on recent and upcoming global requirements to meet your needs.

Contact a Partner today to discover how FlexPro achieves regulatory compliance right the first time.