



The introduction of subcutaneous DMPA (DMPA-SC, brand name Sayana® Press) promises to expand women’s access to family planning options by increasing opportunities for lower-level health workers and even clients themselves to administer injectable contraceptives. Insights from the first introductions can help inform new country experiences and transitions, whether small pilots or scaled delivery. This section discusses results and lessons learned during introduction pilots in four countries and provides recommendations to guide future efforts by ministries of health and implementing partners related to **product registration**.

PERMISSION TO BUY, IMPORT, AND USE PRODUCT IN A COUNTRY

Registering a new product like Sayana Press (Pfizer’s branded DMPA-SC product) with a country’s relevant drug regulatory authorities is essential for introduction. The national medicines regulatory authority is often a division of the ministry of health (MOH) established to ensure the safety of all medicines on the market. This group monitors the quality and efficacy of all medicines as a public health responsibility; oversees the licensing, trade, and advertising of medicines; and ensures conformity to international legal standards pertaining to the regulation of medicines.

REGISTRATION PROCESSES AND RESPONSIBILITY

Registration influences many ensuing steps in the introduction process. In most cases, a country’s regulatory authority examines available clinical data to evaluate the safety, efficacy, and quality of the product. When review is complete, it issues authorization to import and distribute the product. Registration is required for product procurement and importation, and it drives subsequent modifications to how the product is used.

As the product’s manufacturer, Pfizer Inc. is responsible for Sayana Press registration. In other words, Pfizer must prepare, submit, and track regulatory submissions; determine in

which markets the product should (or can feasibly) be registered, factoring in global health priorities and country demand; and assess how many registration dossiers can be prepared, submitted, and tracked in a given time period. The company must weigh the costs required to register a product like Sayana Press in a new market against the advantages, which are measured in terms of revenue, profit, competitive position, and/or potential benefit to—and demand from—women.



INTRODUCTION TIP

The product manufacturer, Pfizer Inc., leads registration of Sayana Press.

Sayana Press received stringent regulatory approval in 2011 from the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) (see Sayana Press registration milestones box). Stringent regulatory approval is the registration of a new product with one or more regulatory authorities recognized globally as having high standards, such as the UK MHRA, the US Food and Drug Administration (FDA), or the drug regulatory authorities of several other European countries as well as Japan and Australia. The UK MHRA was a critical reference point for the national registration processes in the pilot introduction countries—Burkina Faso, Niger, Senegal, and Uganda.



INTRODUCTION TIP

Sayana Press has stringent regulatory approval from the United Kingdom—including for self-injection—that serves as a key reference point for registrations in other countries.

One question that arose often from global and national stakeholders during the pilot phase is whether Sayana Press should be prequalified by the World Health Organization

(WHO). Like stringent regulatory approval, WHO prequalification can sometimes help streamline national registration processes. Reproductive health procurement agencies do not typically require the products that have been approved by an internationally recognized stringent regulatory authority to also be prequalified by WHO.

In some cases, as an alternative to official registration, Sayana Press has been made available in a country based on a waiver. A waiver is a type of interim regulatory approval granted for a limited time frame concurrent with the full regulatory approval process. Waivers are often requested for a specific purpose such as a small pilot or trial. For example, Sayana Press was initially made available via the waiver process in Malawi, for the purposes of a self-injection study, and in the Democratic Republic of the Congo because of complexities and lengthy timelines associated with country-level regulatory approval.



INTRODUCTION TIP

Waivers are an option if country registration processes might delay product introduction substantially.

UNPREDICTABILITY OF REGISTRATION TIMELINES

Product registration for the first four Sayana Press pilot introductions was complex and time-consuming. Because the registration application process is driven by Pfizer and depends on country regulatory processes, it is the part of the introduction process over which implementing organizations have the least control. Preparation for regulatory submissions alone can require considerable resources. For example, after the July 2012 London Summit on Family Planning and the commitment of donor resources to Sayana Press pilot introduction, it took about six months for Pfizer to prepare multiple, simultaneous regulatory submissions for diverse country systems. National regulatory submissions were made in Burkina Faso, Niger, Senegal, and Uganda in early 2013.

Sayana Press registration milestones.

Since 2007, the safety, efficacy, and quality of Sayana Press and the drug contained in Sayana Press (DMPA-SC [generic name for the subcutaneous form of depot medroxyprogesterone acetate]) have been thoroughly vetted through multiple steps in the registration process.

- **2007: Sayana receives stringent regulatory approval from the UK MHRA.** Sayana is the same drug that is used in Sayana Press, but it is packaged in a glass, prefilled syringe for administration by a health worker. Pfizer's approved registration with the MHRA permitted additional country registrations in Europe through a "cascade" to other European Union countries that have a mutual recognition agreement for drug regulatory approvals with the MHRA.
- **2011: Sayana Press receives stringent regulatory approval from the UK MHRA,** based on an amendment to the original Sayana registration. The amendment requested regulatory approval of a container change: Sayana in the Uniject injection system (formerly known as depo-subQ in Uniject, now known as Sayana Press).
- **2013–ongoing: Sayana Press receives national regulatory approval in Burkina Faso, Niger, Senegal, and Uganda and beyond.** With stringent MHRA approval of Sayana Press in place, Pfizer filed for regulatory approval in more individual countries, including the four pilot countries. The submission requirements, timelines, and processes for review and approval in each country varied.
- **2015: Sayana Press self-injection approved by the UK MHRA.** Based both on commercial and global health interest, Pfizer prepared additional regulatory documentation on the safety and efficacy of self-injection, referencing studies undertaken in the United States and the UK. Pfizer submitted a new application to the MHRA to update the Sayana Press label to include self-injection as an additional route of administration, which was approved in 2015.
- **2016–ongoing: Sayana Press self-injection label approved by national regulatory authorities in Niger, Uganda, and beyond.** The MHRA's approval of Sayana Press for self-injection is now facilitating submission, review, and approval of a set of country-level applications for label updates. Niger was the first country to have national regulatory approval for the new product label.



INTRODUCTION TIP

While implementers are not directly involved in product registration, they can check with authorities and see how it is going. On occasion, implementers may be able to assist in resolving problems that stakeholders or regulators are not aware of.

In the four pilot countries, the time from Pfizer's regulatory submission to national regulatory approval varied from just six weeks to more than a year. If effective coordination mechanisms are in place, planning for introduction can proceed while product registration is in process. For example, PATH continued to revise and review DMPA-SC training curricula with the MOHs and engaged local partners to plan provider training and

behavior change communication activities. In addition, PATH DMPA-SC coordinators and key ministry representatives helped track each step of the registration process, identify bottlenecks, and keep the process moving, to a certain extent.

Still, final implementation of certain country-level activities was delayed given uncertainty about the timing of the product's arrival in country. Flexibility in developing work plans and perseverance are keys to successful project implementation. For example, provider training was planned but not scheduled until the product was in country and available for distribution. Launch events were planned with official dates on hold pending final regulatory approval and certainty of the product's arrival in the country. Success in navigating these unpredictable timelines during the pilots reflects the value of coordination to keep stakeholders informed and activities moving forward.

RECOMMENDATIONS: REGISTRATION

PATH/Gabe Blenczycki



- **Get up to speed on the status of DMPA-SC registration globally.** Know that the safety, efficacy, and quality of this product have been thoroughly vetted. Understanding key facts about the product’s regulatory history—that the drug is approved in the United States and Europe, and that it is approved for self-injection by a stringent regulatory authority—can be useful for navigating many steps in the introduction process.
- **Build flexibility into introduction plan timelines.** Registration is the manufacturer’s responsibility, and national processes are often unpredictable. National product registration processes often take much more time than expected.
- **Track the registration process and know what can be done to move introduction forward in the meantime.** While waiting for registration, it is helpful to stay in touch with key MOH staff and the manufacturer’s point person, in case questions or obstacles arise that require coordination. Introduction planning activities such as design of the monitoring system, revision or development of a provider training curriculum, and conceptualization of communication campaigns can begin before registration is in hand.



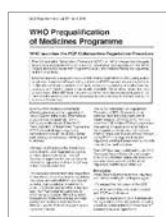
WHO's Essential Medicines and Health Products Information Portal.

Available at apps.who.int/medicinedocs/en/. This website portal serves as a repository for full-text articles about all aspects of international drug and health product registration.



Access to Medicines and Drug Regulation in Developing Countries: A Resource Guide for DFID.

Available at apps.who.int/medicinedocs/documents/s18246en/s18246en.pdf. This paper provides an overview of the debate about how developing country drug regulation agencies are funded and the extent to which they should build local capacity or rely on regulatory bodies in developed countries.



WHO Launches the PQP Collaborative Registration Procedure.

Available at apps.who.int/medicinedocs/en/d/J/s21317en/. This concise summary of WHO's Collaborative Registration Procedure describes the advantages of this program as well as experiences and lessons learned during the launch of the activity in 2012.



WHO Collaborative Registration Procedure for Medicines in Developing Countries. Master's Dissertation.

Available at dgra.de/media/pdf/studium/masterthesis/master_haas_s.pdf. This thesis provides an in-depth review of key WHO-led procedures for registering medicines in developing countries, including prequalification, the concept of essential medicines, and collaborative registration.