

Home-based administration of depo-subQ provera 104™ in the Uniject™ injection system

A LITERATURE REVIEW

Bonnie Keith



ACKNOWLEDGMENTS

This document was written by Bonnie Keith with key contributions from Jane Hutchings, Sara Tifft, and Siri Wood, and was designed by Patrick McKern. PATH would like to acknowledge the support of the Bill & Melinda Gates Foundation for this project.

Copyright © 2011, Program for Appropriate Technology in Health (PATH). All rights reserved. The material in this document may be freely used for educational or noncommercial purposes, provided that the material is accompanied by an acknowledgment line.

Suggested citation:

Keith, BM. *Home-based Administration of depo-subQ provera 104™ in the Uniject™ Injection System: A Literature Review*. Seattle: PATH; 2011.

CONTACT INFORMATION

MAILING ADDRESS

PO Box 900922
Seattle, WA 98109 USA

STREET ADDRESS

2201 Westlake Avenue, Suite 200
Seattle, WA 98121 USA

info@path.org
www.path.org

Contents

Acronyms.	ii
Introduction	1
Overview of injectable contraception	1
Injectable formulations	2
Depot medroxyprogesterone acetate (DMPA)	2
Depo-subQ provera 104™ in the Uniject™ injection system	4
Overview of non-clinic access to injectables.	6
Administration by lay caregivers	7
Administration by self-injection	7
Considerations for home delivery of depo-subQ in the Uniject system in low-resource settings	9
Training	9
Storage	10
Safe injection and waste management	11
Infrastructure	12
Political support	12
Conclusion and next steps	12
References	13

Tables

Table 1: Injectable contraceptives—Formulations and injection schedules	2
Table 2: Associated benefits and side effects of DMPA use	3
Table 3: Comparison of advantages for subcutaneous and intramuscular injections	4
Table 4: Benefits of the Uniject injection system	5

Acronyms

BMD	Bone mineral density
CBD	Community-based distribution
CHW	Community health worker
DMPA	depot medroxyprogesterone acetate
IM	Intramuscular
NET-EN	Norethisterone enanthate
SC	Subcutaneous
UNFPA	United Nations Population Fund
USAID	United States Agency for International Development
WHO	World Health Organization

Introduction

With funding from the Bill & Melinda Gates Foundation, PATH is implementing a four-year project to facilitate decision-making and introduction strategies for depo-subQ provera 104™ in the Uniject™ injection system (depo-subQ in Uniject), a new subcutaneous formulation of the injectable contraceptive depot medroxyprogesterone acetate, or DMPA.* The Uniject delivery system is a prefilled, autodisable injection device containing one dose offering three months of contraceptive protection. Introduction of depo-subQ in Uniject in developing countries may provide opportunities to both strengthen clinic injection services and extend injectable contraceptive delivery safely and effectively beyond the clinic.

The goal of PATH's *Planning for Introduction of depo-subQ provera 104™ in the Uniject™ Injection System* project is to accelerate global and country-level introduction of depo-subQ in Uniject. PATH is working to achieve this goal through five objectives:

1. Generate relevant data and experience to inform evidence-based introduction and scale-up.
2. Prepare and present information and analyses to support introductory product procurement.
3. Facilitate decision-making and introduction planning in up to five focus countries.
4. Stimulate global support for the product and introduction planning.
5. Lead coordination of global partners supporting global product rollout.

The project's outputs will provide information to global and country-level decision-makers involved in programming for family planning services in the public, nongovernmental, social marketing, and commercial sectors. The information will be used to aid them in determining whether and how to introduce depo-subQ in Uniject into their family planning programs. More specifically, PATH is working closely with country advisory groups in Kenya, Malawi, Pakistan, Rwanda, and Senegal to help prepare detailed country introduction plans for depo-subQ in Uniject.

To identify family planning service delivery settings where depo-subQ in Uniject might add the most value by increasing access and use, PATH has conducted various analyses. One component of this part of PATH's work is to

*For the purposes of this review, "DMPA" references all formulations of depot medroxyprogesterone acetate, including DMPA SC. "DMPA IM" refers to depot medroxyprogesterone acetate administered intramuscularly, while "DMPA SC" refers to depot medroxyprogesterone acetate administered subcutaneously. "Depo-subQ" references Pfizer's brand-name DMPA SC product.

conduct research assessing the feasibility and acceptability of home delivery of depo-subQ in Uniject with a focus on self-injection as a service delivery mechanism for injectable contraceptives. The present literature review will inform the design and implementation of this research, which will, in turn, be used to inform country introduction strategies for depo-subQ in Uniject.

The objectives of this paper are to:

- Review the available literature on subcutaneous DMPA and compare the subcutaneous and intramuscular formulations of DMPA.
- Review the available literature on home administration of injectable contraception, focusing on the feasibility and acceptance of self-injection, particularly in low-resource countries.
- Identify evidence and knowledge gaps and describe future research needs regarding home and self-injection of depo-subQ in Uniject.

The review provides background on injectable contraceptives, describes the depo-subQ in Uniject product, and presents experience and evidence regarding non-clinic access to injectables. These elements build a picture of the delivery continuum and highlight issues that are important to consider when planning for introduction of a new method. With these components as a backdrop, the review then examines the issue of home and self-injection using depo-subQ in Uniject. The review addresses a broad range of considerations for home and self-injection from training, storage, and waste management to infrastructure and political support.

Overview of injectable contraception

Injectable contraceptives (injectables) are one of the world's most popular modern methods of contraception. Many women prefer injectables to other modern methods because of their effectiveness, long-acting contraceptive effects, discreet administration, and reversibility. Globally, injectable contraceptives are the fourth most popular method of contraception (after female sterilization, intrauterine devices, and oral contraceptive pills).¹ Demand for injectables is increasing most rapidly in sub-Saharan Africa, where they account for 38 percent of modern contraceptive use.^{1,2} Estimates suggest global use of injectables will increase to almost 40 million users by 2015, a 31-percent increase from 2000 levels according to the United Nations Population Fund (UNFPA). These expected increases call for sustained access to injectable services and supplies.^{1,3}

The recent growth in use of injectables is largely due to increased access and expanded family planning programming focused on injectables. These factors will continue to contribute to future injectable growth. In particular, increased access is expected to expand further through community-based distribution (CBD), the private commercial sector, social marketing programs, and, eventually, self-injection at home.¹

INJECTABLE FORMULATIONS

Injectable contraception is available in one-, two-, or three-month administration intervals, based on the specific formulation. As of September 2009, there were eight different formulations of injectable contraception available globally. A comprehensive list is included in Table 1.

Family planning programs in developing countries usually offer a progestin-only injectable such as DMPA or NET-EN (norethisterone enanthate), and some may also provide combined injectables (progestin plus estrogen).^{1,5,6} Family Health International data from 2008 suggests

approximately 14 million women worldwide use DMPA, making it the most widely available and most commonly used injectable formulation.⁶

DEPOT MEDROXYPROGESTERONE ACETATE (DMPA)

Depot medroxyprogesterone acetate, or DMPA, is a progestin-only, aqueous suspension (water-based) injectable contraceptive. DMPA is effective for three months, is completely reversible, and also has a lenient four-week grace period for users unable to return for follow-up injections on their scheduled reinjection date.^{7,8} These are some of the reasons why DMPA is the most popular injectable contraceptive; others include its low cost, global use, and availability in both branded and generic forms. Table 2 shows the benefits and side effects associated with DMPA use.

DMPA has been available from various manufacturers for more than 40 years. It is a widely approved method of contraception, with drug regulatory agencies in more than 179 countries having approved its use.^{10,11} It is

TABLE 1: Injectable contraceptives—Formulations and injection schedules

Common trade names	Formulations	Injection type and schedule
<i>Progestin-only injectables</i>		
Depo-Provera [®] , Megestron [®] , ^a Contracep [®] , Depo-Prodason [®] , Petogen [®]	Depot medroxyprogesterone acetate (DMPA) 150 mg	One intramuscular (IM) injection every three months
depo-subQ provera 104™ (DMPA SC)	DMPA 104 mg	One subcutaneous injection every three months
Noristerat [®] , Norigest [®] , Doryxas [®]	Norethisterone enanthate (NET-EN) 200 mg	One IM injection every two months
<i>Combined injectables (progestin + estrogen)</i>		
Cyclofem [®] , Ciclofeminina [®] , Lunelle [®]	Medroxyprogesterone acetate 25 mg + Estradiol cypionate 5 mg (MAP/E2C)	One IM injection every month
Mesigyna [®] , Norigynon [®]	NET-EN 50 mg + Estradiol valerate 5 mg (NET-EN/E2V)	One IM injection every month
Deladroxate [®] , Perlutal [®] , Topasel [®] , Patectro [®] , Deproxone [®] , Nomagest [®]	Dihydroxyprogesterone acetophenide 150 mg + Estradiol enanthate 10 mg	One IM injection every month
Anafertin [®] , Yectames [®]	Dihydroxyprogesterone acetophenide 75 mg + Estradiol enanthate 5 mg	One IM injection every month
Chinese Injectable No. 1 [®]	17 α -hydroxyprogesterone caproate 250 mg + Estradiol valerate 5 mg	One IM injection every month, except two injections in the first month

^a Megestron is no longer in production.

TABLE 2: Associated benefits and side effects of DMPA use^{1,4,7}

Benefits	Side effects
<ul style="list-style-type: none"> • Immediate^a and highly effective protection from pregnancy • Decreased risk of iron-deficiency anemia (due to associated amenorrhea) • Protection against endometrial cancer and uterine fibroids • Reduced sickle cell crises in women with sickle cell anemia • Ability to use while breastfeeding 	<ul style="list-style-type: none"> • Menstrual irregularities • Weight gain • Delayed return to fertility^b • Mineral bone density loss^c

^a DMPA is immediately effective if administered during the first five days of a woman's menstrual cycle. If administered after the first five days of a menstrual cycle, it takes three days to become effective.

^b The average woman is fertile within 10 months after their last injection.⁷

^c As noted by the World Health Organization (WHO), "...data indicates that DMPA reduces bone mineral density (BMD) in women using DMPA who have attained peak bone mass, and impairs the acquisition of bone mineral among those who have not yet attained peak bone mass.... when DMPA use is discontinued, BMD increases again in women, regardless of age, except for those who have reached menopause." The WHO recommends that there should be no restrictions on the use of DMPA, including restricting the duration of use, for women age 18-45 years who are otherwise eligible to use the method.⁹

provided in numerous countries through both national procurement and donor support, including the United States Agency for International Development (USAID), UNFPA, and the International Planned Parenthood Federation. USAID exclusively procures DMPA over other injectable formulations for USAID-supported family planning programs.

Historically, DMPA has been administered via an intramuscular (IM) injection in the upper arm using a vial and autodisable syringe. This route of administration has been highly acceptable in many countries, as many providers are already competent in intramuscular injection of other medicines. Over the years, countless clinical staff have received training in provision of DMPA IM, learning skills in injection, storage, waste disposal, screening for contraindications, and counseling on management of side effects. In an effort to increase access to injectable contraception, a number of countries in Africa are training community-based health workers to provide DMPA to women in areas that are difficult to reach, especially in rural settings. This approach is based on past successes with CBD of injectables in Bangladesh, Guatemala, Nepal, and other countries.¹² Expanding non-clinic access to injectables has greatly expanded the coverage of family planning services while simultaneously building the capacity of the community health workers (CHWs).

Intramuscular vs. subcutaneous DMPA

In 2004, the United States Food and Drug Administration approved Pfizer Inc.'s new formulation of DMPA, depo-subQ provera 104.⁷ According to Pfizer labeling, subcutaneous (SC) DMPA is administered through a subcutaneous injection in a woman's thigh or abdomen

using a prefilled, single-use syringe.¹³ Because DMPA SC is administered subcutaneously, the progestin is absorbed more slowly in the body, allowing for a lower dose of the hormone compared with DMPA IM (DMPA SC contains 104 mg of progestin vs. 150 mg in DMPA IM). Despite containing only 70 percent of the active ingredient, DMPA SC is equally as effective as DMPA IM in suppressing ovulation and thereby preventing pregnancy.^{14,15,16,17} Pfizer has supported and/or participated in a number of DMPA SC contraceptive-effectiveness studies,* subsequently published in independent peer review journals. These studies have shown a zero percent pregnancy rate after one and two years of use, according to Jain et al. and Kaunitz et al., respectively.^{15,17} Research also suggests that efficacy of the DMPA SC formulation is unaffected by race, ethnicity, or body mass.^{15,16,17}

It is important to highlight that DMPA SC is a new formulation of depot medroxyprogesterone acetate; therefore, a smaller amount of DMPA IM cannot be injected subcutaneously and still be effective. Conversely, DMPA SC is not effective if injected intramuscularly.⁸ Because DMPA SC is only available in a prefilled syringe, the likelihood of provider confusion between the two formulations is negligible.

*Jain J, Dutton C, Nicosia A, et al. Pharmacokinetics, ovulation suppression and return to ovulation following a lower dose subcutaneous formulation of Depo-Provera. *Contraception* (2004); 70:11-18. Jain J, Jakimiuk AJ, Bode FR, et al. Contraceptive efficacy and safety of DMPA SC. *Contraception* (2004); 70:269-75. Toh YC, Jain J, Rahimy MH, et al. Suppression of ovulation by a new subcutaneous depot medroxyprogesterone acetate (104 mg/0.65 mL) contraceptive formulation in Asian women. *Clinical Therapeutics* (2004); (26)11:1845-54. Kaunitz AM, Darney PD, Ross D, et al. Subcutaneous DMPA vs. intramuscular DMPA: a 2-year randomized study of contraceptive efficacy and bone mineral density. *Contraception* (2009); 80:7-17. Arias RD, Jain JK, Brucker C, et al. Changes in bleeding patterns with depot medroxyprogesterone acetate subcutaneous injection 104 mg. *Contraception* (2006); 74:234-38.

Side effects of DMPA SC are consistent with those known for other progestin-only injectable contraceptives, including DMPA IM (see Table 2).¹⁷ According to the available research, frequent side effects associated with DMPA SC include: headache, weight gain, intermittent bleeding and spotting, and amenorrhea.^{14,15,17,18,19} In a two-year, randomized, Phase III comparison study between DMPA SC and DMPA IM among 225 women in Brazil, Canada, and the United States, Kaunitz and colleagues found that side effects were similar in both study groups. Kaunitz et al. also found that “...the incidence of treatment-emergent adverse events (i.e., events that developed for the first time after initiation of treatment or events that were already present but worsened in either intensity or frequency following initiation of treatment) occurring in ≥ 5 percent of women was similar between the groups and reflected the known adverse-event profile of DMPA.”¹⁷ The only statistically significant difference between the two groups was an increase in injection-site reactions in the group receiving DMPA SC (8 percent vs. 0.4 percent of DMPA IM users), all of which were reported as mild to moderate reactions. In this study, the primary reason for discontinuation of DMPA use for both groups was weight gain (13 percent for DMPA SC users and 15 percent for DMPA IM users).

One critical side effect of DMPA use is changes in bleeding patterns. Women frequently cite these changes as a reason for method discontinuation. DMPA SC appears to have the same effect on bleeding patterns as DMPA IM; specifically, irregular bleeding and spotting decrease over time while incidence of amenorrhea increases correspondingly.^{15,17,19} In an analysis of bleeding-pattern changes in women using DMPA SC, Arias and colleagues found that 51 percent of women experience bleeding or spotting in the month after the first injection.¹⁹ Incidences of bleeding or spotting gradually decreased over the course of the study, with the percentage of women shifting from bleeding or spotting to amenorrhea increasing with each succeeding injection. By the end of the second year, 71 percent of the women studied reported amenorrhea.¹⁹

While the clinical profiles of DMPA SC and DMPA IM are roughly equivalent, many authors suggest that DMPA SC may offer advantages over DMPA IM.^{14,16,17,20,21} In addition to a lower hormone dose, these advantages include ease of administration, potential for self-injection, and increased long-term tolerability.²¹ Both Toh et al. and Kaunitz et al. note the potential for “ease of administration” provided by a subcutaneous injection.^{16,17} In a general assessment of intramuscular injections versus subcutaneous injections, Prettyman notes that administration of subcutaneous injections

“may be easier” than intramuscular injections because, with intramuscular injections, the provider must be familiar with “anatomical landmarks.”²⁰ Additionally, providers have more surface area to work with when administering subcutaneous injections in sites such as the thigh or abdomen. Prettyman’s discussion states that subcutaneous injections can cause less distress than intramuscular injections because the needles used for subcutaneous injections are smaller in both gauge and length. Moreover, she further notes that subcutaneous injections are less likely than intramuscular injections to pierce blood vessels, hit nerve endings, or make contact with bone (due to the shorter needle length). Table 3, taken from Prettyman’s review, compares the general advantages of subcutaneous and intramuscular injections.

TABLE 3: Comparison of advantages for subcutaneous and intramuscular injections²⁰

Subcutaneous advantages	Intramuscular advantages
<ul style="list-style-type: none"> • Greater area for target injection sites • Fewer landmarks required for targeting injection sites • Shorter needles can be used (3/8 to 5/8 inch) • Readily self-administered • Good for multiple dosing • Muscle mass not an issue 	<ul style="list-style-type: none"> • Can give greater volume of drug product (2 to 5 mL) • Drugs irritating to subcutaneous tissue may be given intramuscularly

DEPO-SUBQ PROVERA 104™ IN THE UNIJECT™ INJECTION SYSTEM

Currently, DMPA SC is exclusively manufactured by Pfizer Inc. under the brand names depo-subQ provera 104 and Sayana®. DMPA SC is presently available in a glass, prefilled syringe as depo-subQ provera 104 in the United States and Sayana outside of the United States. Pfizer is working with BD (Becton, Dickinson and Company), the makers of the Uniject injection system, to manufacture depo-subQ* in Uniject.

*Depo-SubQ Provera 104 is the manufacturer’s name for DMPA SC. When referencing the Pfizer product specifically, rather than the drug, the term ‘depo-subQ’ will be used. Please note that until Pfizer’s patent expires and other manufacturers begin to make DMPA SC, depo-subQ will be the only form of the drug available.



PATH/Patrick McKern

The Uniject injection system.

Uniject is designed with a plastic blister filled with a single dose of medication for injection.²² This design simplifies both storage and training. The provider administering the injection resuspends the depo-subQ by shaking the Uniject for 30 seconds, depresses the cap to activate the device, inserts the needle into the skin, and squeezes the blister to administer the full dose. A one-way valve prevents the device from being refilled, thereby reducing the risk of reuse or infection transmission. Table 4 highlights key benefits of the Uniject injection system.

While depo-subQ is the newest drug available in Uniject, the device has been used to deliver a number of medications and vaccines, including Cyclofem®, a monthly injectable contraceptive; hepatitis B vaccine; tetanus toxoid vaccine; and oxytocin for prevention of postpartum hemorrhage.²² Providers delivering vaccines and medication via Uniject have included nurses, midwives, CHWs, and self-injectors.^{23,24,25,26,27} In a study conducted in Brazil, researchers determined that Uniject is “... appropriate for the delivery of...injectable contraceptives.”²⁴

Non-clinic experience with the Uniject injection system

There are a variety of studies assessing non-clinical use of Uniject. Three studies reviewed home delivery of medicines in Uniject in Indonesia and the researchers found the delivery system to be simple, easy to learn, practical, cost effective, and safe.^{25,26,27} The providers assessed in these studies were all village midwives who received training in administration and storage of Uniject and the medicine contained therein. In one study, assessing the delivery of tetanus toxoid and hepatitis B vaccines via Uniject, researchers found that midwives and clients readily accepted the device; in fact, mothers of the children receiving the vaccines expressed preference for Uniject delivery and were disappointed when subsequent vaccines were delivered via a standard

TABLE 4: Benefits of the Uniject injection system²²

Ease of use	Allows use by trained lower-level health workers and offers the potential for self-injection
Prefilled single unit	Ensures that the correct dose is given, simplifies procurement and logistics, eliminates the need to bundle vials and syringes, and prevents their potential mismatch at service delivery points
Not reusable	Minimizes transmission of blood-borne pathogens through needle reuse
Compact size	Eases transport, storage, and disposal

syringe.²⁵ A study of midwives providing oxytocin to new mothers via Uniject found that use of the device increased the accuracy of dosing as well as injection safety.²⁶ Prior to the study, 51 percent of the midwives reported previously using syringes and needles more than once. Midwives and their clients reported high levels of satisfaction with the device, and the researchers concluded that provision of oxytocin in Uniject is “...a feasible option for use in the home by trained midwives.”²⁶

As noted in the previous paragraph, past research has concluded that provision of medicines and vaccines via Uniject is highly satisfactory to both providers and recipients.^{25,26} In a study assessing the use of the monthly injectable contraceptive Cyclofem in the Uniject injection system, both provider and user perceptions were highly positive.²⁴ Eighty percent of providers stated that they would prefer to use Uniject over another type of syringe in the future, if available, and 94 percent of the women receiving the injections said they would gladly receive Uniject injections in the future.²⁴

The evidence presented here suggests that Uniject is an acceptable delivery mechanism for medicines, including injectable contraceptives. There is also clear evidence demonstrating the successful use of Uniject in the home by appropriately trained providers. Given this evidence and experience, making depo-subQ in Uniject available to CHWs and women interested in home-based injection may offer new modalities for increasing access to family planning, particularly in geographic areas or settings where women may have difficulty accessing regular care at traditional facilities. More broadly, increasing non-clinic access to injectables may also lead to an increase in new users of family planning, helping to reduce unmet need and improve contraceptive prevalence.^{28,29,30}

Depo-subQ in Uniject: Advantages for home use

The possibility for home use of depo-subQ in Uniject is one of the more innovative potential advantages of this injectable contraceptive delivery system. For the purposes of this literature review, the term “home use” refers to administration of depo-subQ in Uniject either by a third party (e.g., a family member) delivering the injection in a woman’s home, or by the woman herself through self-injection. In addition to the general benefits of Uniject presented in Table 4, the availability of depo-subQ in Uniject presents a number of specific advantages for home-based delivery of injectable contraception. Among them:

- **Ease of use:** The simpler techniques associated with delivering depo-subQ via the Uniject injection system can decrease the amount of training time required to become skilled in administration.^{24,31} Moreover, easier administration may also decrease the time required to deliver the injection; a study conducted by PATH and WHO showed that injections via Uniject required four fewer steps than injections using a standard syringe (six steps vs. ten, respectively).³²
- **Accurate dose:** An accurate dose of depo-subQ is already incorporated into Uniject, eliminating concerns over delivering the proper dose.
- **Logistical benefits:** Because Uniject is smaller than a syringe and vial, it is easier to transport and store. A study commissioned by PATH found that depo-subQ in Uniject is 62 percent lighter and 25 percent less voluminous than DMPA IM packed with vial and syringe.³³
- **Waste disposal:** Because Uniject is a small delivery system with minimal packaging, it requires less space in a sharps disposal container than a standard autodisable syringe. A waste management assessment conducted by PATH found that depo-subQ in Uniject generates 70 percent less waste by volume than the standard autodisable syringe (SoloShot®) with an empty DMPA vial.³⁴ Excluding the vial, use of depo-subQ in Uniject generates 39 percent less waste by volume than an autodisable syringe.³⁴

Overview of non-clinic access to injectables

Historically, home delivery of family planning services, including injectable contraceptives, has been provided by CHWs through CBD programs for hard-to-reach populations. While there are multiple CBD program models, most often services are provided in the client’s home through a system known as “doorstep” delivery. There is a large body of evidence suggesting that provision of injectable contraception in a woman’s home by a CHW is acceptable, effective, and satisfactory to both the user and provider.^{12,35,36,37,38,39} CBD of injectables through CHWs has occurred in countries such as Bangladesh, Ethiopia, Guatemala, Madagascar, Mexico, Nepal, and Uganda, among many others.^{12,40} In 2009, a technical consultation hosted by WHO reviewed available literature and program experience and affirmed that CHWs can safely and effectively administer injectable contraceptives, namely DMPA.⁴⁰

Home-based provision of injectable contraceptives through CHWs has greatly expanded women’s

contraceptive options. In a 1997 report on lessons learned from a highly successful CBD project in Bangladesh, Khuda et al. found that home-based provision of injectable contraception (along with oral contraceptives and condoms) vastly expanded the family planning options for women, especially those seeking to space, rather than limit, their pregnancies.³⁸ Moreover, the clients were highly satisfied with the method and accessibility of services.³⁸ In a report on the safety and feasibility of CBD of DMPA IM in Uganda, Stanback et al. suggest that clients of CHWs prefer to receive their injections either in their own home or the home of the CHW as compared with a clinic.³⁷

Successful programs offering CBD of injectables incorporate thorough training focused on screening and counseling clients and safe injection practices, including waste disposal.^{12,36} Regular supervision for CHWs is a hallmark of a successful program, as is reliable, sustainable access to the necessary supplies. Above all, national policies must reflect support for home-based provision of injectables by CHWs.^{12,35,36,37,40} While home delivery of injectables can succeed with these elements in place, there are often times when CBD may be unavailable. CHWs may not visit a community or household as often as

they should, weather conditions may prevent them from reaching their target communities for months at a time, or financial support for home-delivery programs may run out.³⁶ Where CBD services are sporadic or unavailable, the ability to administer injectables in the home by a lay caregiver or through self-injection may offer women more choice in their family planning options and, overall, in controlling their fertility.

ADMINISTRATION BY LAY CAREGIVERS

There is no published literature available on provision of injectable contraception in a woman's home by a lay caregiver, such as a friend or relative. However, research on provision of other medicines suggests this is a feasible option for contraceptives. It is quite common for children with diabetes, for instance, to receive insulin injections in the home from their parents or another caregiver. A successful program in the United Kingdom teaches caregivers to administer methotrexate injections in the home to children with rheumatic disease.⁴¹ After thorough training, the caregivers were able to provide subcutaneous injections in the thigh using a prefilled syringe.⁴¹ Caregivers were very positive about the program and the impact it had on their lives; home provision gave them more freedom because they were required to travel to the clinic less often. In a study assessing caregivers' abilities to deliver subcutaneous injections for pain management in the home, Israel et al. found that caregivers preferred prefilled syringes and that their confidence in administering the injections increased over time.⁴² Similarly, Bevan et al. found that patients with acromegaly (a chronic metabolic disorder) or their partners were safely and effectively able to provide subcutaneous injections at home, employing prefilled syringes.⁴³ In their words, "...unsupervised home injections are a viable alternative to healthcare professional injections for suitably motivated patients."⁴³ In each of these cases, careful selection criteria and thorough training were the keys to ensuring caregivers were confident and skilled in the provision of home-based injections. Moreover, it was important to have a follow-up mechanism when there were questions or a need for further training reinforcement.^{41,42,43}

While the evidence for administration of injectable medicines by lay caregivers is sufficient to suggest they can successfully administer injectable contraception, it should be stated that past experience for lay-caregiver administration of injectable medications probably occurs under different circumstances than those in place for injectable contraception. Users likely need to be injected more often than once every one to three months, and the opportunity to inject at home may also increase compliance with treatment for chronic conditions.

However, the evidence does show that lay caregivers can be trained to administer injections and there are lessons to be learned, despite potential differences in medical regimens. The evidence also shows that lay caregivers are competent in the provision of subcutaneous injections in the home using prefilled syringes.^{41,42,43} Based on the available literature, it can be inferred that, with sufficient training and follow-up, home delivery of depo-subQ in Uniject by lay caregivers is both feasible and acceptable.

ADMINISTRATION BY SELF-INJECTION

Depo-subQ in Uniject increases the possibility for a woman to successfully self-administer a DMPA injection in her own home.^{14,16,17,18,21} While depo-subQ is currently labeled only for administration by a trained clinical provider, WHO, in addition to the previously cited researchers, acknowledges the potential for self-injection associated with DMPA SC.⁷ Kaunitz states: "...self-administered DMPA SC might increase compliance by eliminating the need for women to periodically return to their health care provider for injections."¹⁷ This will be particularly advantageous for those women in remote areas who must travel long distances to their family planning providers. Prettyman remarks that, for self-administration of drugs, subcutaneous delivery is customary.²⁰ Moreover, as stated by Bevan et al., with proper training patients were easily able to self-administer subcutaneous, ready-to-use injections in the thigh, which is the same administration technique suggested for depo-subQ.⁴³

As depo-subQ in Uniject is not yet available for use, there is no published peer-reviewed research on the feasibility and acceptability of self-injection using this



Research suggests that depo-subQ in Uniject increases the possibility for a woman to easily inject herself at home.

particular injectable delivery system. There is in fact no published data on self-injection using any formulation of DMPA. However, information on unpublished results from the broader Jain et al. (2004) study that included a component assessing self-injection of DMPA SC suggests self-injection of this formulation of DMPA may be both feasible and acceptable.²¹ Conference abstracts and personal communications with one of the study's authors suggest that women self-selected the option to self-inject.⁴⁴ Those who chose self-injection received the first injection from a nurse and were trained by the nurse to administer their own follow-up injections and also trained on disposal methods (specifics unknown). Written training materials in the form of a brochure were also available. Women administered the injection in the thigh, though the drug delivery mechanism is not stated. In a symposium presentation sponsored by Pfizer, researchers shared data that suggested self-injectors found it a highly convenient and easily administered form of contraception.²¹ Moreover, 95 percent of self-injectors from the Americas study and 79 percent from the European/Asian study would prefer to continue self-administering DMPA SC if using it in the future.²¹ While this unpublished data on self-injection of DMPA SC suggests potential feasibility of self-injecting depo-subQ in Uniject, peer-reviewed evidence is needed. Two studies on self-injection of DMPA SC using prefilled glass syringes are currently underway in the United States and will provide further evidence on the acceptability and feasibility of self-injecting this contraceptive.

While there is limited information on self-injection of DMPA SC, peer-reviewed, published data on self-injection is available for other formulations of injectable contraception, including administration using the Uniject system.^{45,46} Data from two studies evaluating the acceptance of contraceptive self-injection suggest self-administration of injectable contraception is both feasible and acceptable.^{45,46}

In a 1997 Brazilian study, Bahamondes et al. assessed user ability to self-administer the once-monthly contraceptive Cyclofem® using Uniject. The researchers found that participants were not only able to self-administer their intramuscular contraceptive injection safely and easily, but that over half of them would prefer to self-administer using Uniject in the future.⁴⁵ After receiving thorough training and practicing injections using oranges, participants self-administered their injections in a clinic under the supervision of a nurse. Over 90 percent of the women correctly self-administered their injections with all delivering the injection in the thigh.⁴⁵ Of the participants, 57 percent liked self-injection and wished to administer their contraceptive in their own home. Thirty

percent were confident in self-administration in the clinic setting, but expressed uncertainty over doing so in their own home. The remaining 13 percent felt administration in the thigh was too painful.⁴⁵

In a study conducted in the United States, researchers compared self-injection of the monthly contraceptive Lunelle® in the home to delivery in the clinic, assessing patient satisfaction as well as cost and time variables.⁴⁶ Women were trained to self-inject the contraceptive intramuscularly in the thigh and also received training on sterile techniques and waste disposal. Participants in this study used a standard vial and syringe delivery system rather than a prefilled device.⁴⁶ Of the women completing the study, 80 percent preferred self-injection in the home to clinic administration, even with the standard syringe.⁴⁶ Moreover, the study suggests a cost-savings benefit with home-based self-administration, as the subjects did not need to spend money on transportation, child care, or time away from work when self-administering at home.

It should be noted that the sample size of both study populations was relatively small: 56 women in the Brazil study and ten women in the United States study.^{45,46} However, the results suggest that, with comprehensive training, women are capable of self-administering injectable contraception. Moreover, the women in each of these studies were self-administering intramuscular injections. As discussed previously, the evidence suggests that subcutaneous injections are easier to administer than intramuscular injections.^{14,17,18,20,46,47} Uniject is anticipated to further ease administration (please refer to pages 5-6 and Table 4).

In addition to the applied research on self-injecting contraceptives, Lakha et al. administered a survey to assess the potential acceptance of self-injecting DMPA SC.⁴⁸ In the first study, the researchers administered a questionnaire to current users of DMPA IM visiting a clinic in the United Kingdom. Questionnaire One assessed women's interest in switching from DMPA IM to self-injection of DMPA SC. Sixty-seven percent of respondents reported they would prefer to self-administer their contraception.⁴⁸ Among those who did not desire to change the route of administration, the primary reasons were due to a fear of needles and lack of confidence in their ability to properly self-inject.⁴⁸

In Questionnaire Two, which was administered to current DMPA IM users, non-users, and past users (i.e., all women attending the clinic), 61 percent of respondents stated they would prefer to visit the clinic less often to access their contraceptive supplies and 21 percent said they would consider using DMPA as their contraceptive

method if self-injection was an option.⁴⁸ However, the researchers found that, among respondents, the primary reason for not using or discontinuing use of DMPA IM was the side effects—not the need for quarterly clinic visits. Their conclusion was that the ability to self-inject DMPA might be beneficial to “...as many as half the women choosing this method.”⁴⁸ Moreover, the researchers concluded that women who wish to self-administer their injectable contraception should be given appropriate training, administering their first injection with clinic supervision and self-injecting the remaining three doses (of an annual supply) at home afterward.

There is certainly enough historical evidence to suggest that self-administration of medicines is acceptable and even routine for some users. Self-injection is common for patients with conditions such as diabetes, multiple sclerosis, infertility, and Addison’s disease. In a commentary on the self-administration of injectable contraceptives, Prabhakaran also reviews the available literature on self-injection. She states:

...patients currently self-inject many medications, including enoxaparin, epinephrine, heparin, sumatriptan, erythropoietin, insulin, gonadotropins, and human recombinant parathyroid hormone. Reports in the literature demonstrate good clinical effectiveness, safety, and patient satisfaction with self-injection.⁴⁷

Prabhakaran’s review of the literature leads her to conclude that “...self-administration of subcutaneous injections is feasible”, and this reviewer would concur.⁴⁷ Based on the literature reviewed, self-administration of depo-subQ in Uniject is anticipated to be both feasible and acceptable to women.

Considerations for home delivery of depo-subQ in the Uniject system in low-resource settings

As noted in the previous section, there is a large body of evidence suggesting that administration of injectable medicines is both feasible and acceptable when delivered by lay caregivers or through self-administration. There is also sufficient evidence to suggest that administering injectable contraceptives via Uniject is feasible and acceptable. After taking all of the existing evidence into account, a number of considerations emerged that may need to be addressed for successful home delivery of depo-subQ in Uniject, particularly for self-administration. Focusing on self-injection, this section will assess a range



Richard Lord

Home delivery of depo-subQ in Uniject can improve family planning access and choice, allowing women and men greater control over the size of their families.

of likely considerations, including training requirements, storage and waste disposal needs, and infrastructure and policy concerns associated with home delivery of injectable contraceptives in low-resource settings.

TRAINING

As noted throughout this review, other experience and evidence indicate that the training curriculum for a depo-subQ in Uniject home-delivery program would need to contain follow-up and supervision components. In the available literature on self-injection, the majority of the training practices include an initial training on self-injection led by a skilled clinician; at least one follow-up session in a facility, where the trainee self-administers their injection under the supervision of the trainer or another skilled provider; and a system for asking questions or receiving support and counseling once training is complete.^{41,45,46,49,50} Training content for CHWs, for example, includes not only typical training topics such as client eligibility and injection safety considerations, but also preparation for supervision and ongoing follow-up.

While skilled personnel, such as CHWs, may only need limited training on administration of the Uniject injection system, the literature suggests that individual home users may require more instruction in order to acquire confidence in delivering injections using aseptic techniques, as well as knowledge on proper storage, waste disposal, and side-effects management.^{25,26,51} In the Bahamondes study, self-injector participants were trained by nurses on the intramuscular use of Uniject and were offered retraining at each follow-up visit.⁴⁵ Of the women who were invited to participate in the study, 31 percent were trained, but subsequently decided not to self-administer because they were "...afraid of the procedure."⁴⁵ Similar numbers were seen in the Lakha survey, in which 33 percent of women surveyed said they would not like to self-administer DMPA SC, primarily because of a fear of needles.⁴⁸ These two studies assessing self-injection of injectable contraception indicate that roughly half of the women approached will follow through with training and self-injection at home.

In the Livermore review, researchers found that most trainees called a dedicated hotline with questions at least once after completing their training.⁴¹ In the examples presented on home and self-injection, trainees were injecting themselves daily, at least once weekly, or monthly.^{41,43,45,49,50} Because depo-subQ requires injections every three months, it may be especially important to evaluate the extent to which self-injectors will retain their learning in the time between injections, both with and without a supportive system that allows for follow up.

The three-month interval between injections suggests that a woman may need especially clear guidance and possibly tools to help remember the timeframe for her next injection. In the Lakha survey, 89 percent of respondents felt they would need reminding of the date for subsequent injections if they chose self-administration. Options the women gave included giving them the dates for follow-up injections at their annual visit, mailing a letter, or sending a text message.⁴⁸ In the developing world, many of these options may not be feasible. However, the training curriculum could be adapted to incorporate the best reminder option for the setting.

It is likely that a successful depo-subQ in Uniject self-injection program will require a long-term implementation period that focuses on training self-injectors in a facility or their home over multiple injection cycles. It may take as long as one year (or four injection cycles) of training and follow up for a woman to become confident and proficient in administering her injections. For example, the training program could be outlined as follows: one training in the facility/home, one supervised self-injection in the clinic/home, and two subsequent unsupervised self-injections in the home demonstrating

retention of self-injection techniques, with access to a CHW or clinician for support as needed. The study of self-injection of Cyclofem using Uniject considered users competent if they successfully administered three consecutive injections—one per month over a three-month period.⁴⁵

These considerations demonstrate the need for thoughtful, clearly developed training protocols for self-injection using depo-subQ in Uniject. Developing robust selection criteria for the enrollment of appropriate clients in a self-injection training program can help mitigate potential challenges.^{41,42,43} For example, training health workers to identify clients who may be good candidates for self-injection and are likely to be continuing users may increase the effectiveness of the training program and preclude unnecessary discontinuation of the method.

STORAGE

A key component of a successful home injection program for depo-subQ in Uniject will be ensuring participants are knowledgeable and comfortable with the storage protocols for the drug. This applies to CHWs who may store the contraceptive in their homes as well as lay caregivers and self-injectors who may need to safely store the drug in their homes between injections. Pfizer recommends that depo-subQ provera 104 (in a prefilled glass syringe) be stored in controlled temperatures between 20° to 25° C (68° to 77° F).¹³ These are the same storage recommendations that apply to the intramuscular version of DMPA.⁵² Pfizer packaging for both the intramuscular and subcutaneous formulations of DMPA does not require refrigeration or maintenance of cold-chain procedures. Currently, DMPA IM manufactured by Pfizer in Belgium is labeled with a five-year shelf life, and depo-subQ in Uniject is expected to have the same shelf life.⁵³

In the Tsu et al. study assessing home delivery of oxytocin in Uniject in Indonesia, midwives stored their oxytocin supplies in their homes for up to one month. Oxytocin requires a storage temperature of 2° to 8° C, but is validated for storage outside these temperatures for up to three months.²⁶ In similar studies in Indonesia, Ott et al. and Sutanto et al. reviewed the success of administration of a home-delivered dose of hepatitis B via the Uniject system. The hepatitis B vaccine is considered heat stable, and the midwives were able to store the vaccine in Uniject in their homes for one month.²⁵ In both studies, the midwives were able to successfully store the medications in their homes without compromising viability.^{25,26,50} These experiences with storing medicines in Uniject suggest it is possible to store them in the home while maintaining effectiveness of the drugs. While studies of this nature have not yet been conducted with depo-

subQ in Uniject, a similar outcome might be expected given that depo-subQ can be stored at much higher temperatures than either the oxytocin or hepatitis B drugs reviewed here.¹³

The previous examples suggest that CHWs with regular access to health facilities for resupply will be able to safely store depo-subQ in Uniject in their homes between client visits. However, there are no examples of storage practices for women living in low-resource settings who are interested in self-injecting their contraceptive method and may not have regular access to health facilities for resupply. Ideally, a woman who wishes to self-administer depo-subQ in Uniject would visit her provider annually and be provided with a year's supply of injectables at that time (three injectables, assuming she receives one during her annual visit). It may be necessary to assess the conditions under which women in developing countries would store these devices in their homes over the course of a year.

Since many women choose to use injectable contraceptives because they are discreet,⁷ it will also be important to assess whether a woman who wishes to self-inject can store the Unijects in a private space that is also temperature appropriate and secure. Another option would be for self-injectors to acquire their depo-subQ in Uniject from their local pharmacy or drug shop shortly before their next scheduled injection, thereby storing it in their home for a shorter time period. This scenario would require private-sector availability of depo-subQ in Uniject, accessible pharmacies or drug shops, and affordable pricing for the consumer. Similarly, a woman who wishes to self-inject could also obtain supplies from her local CHW. Under these circumstances in which a CHW might as easily administer the injection, the advantages of self-injection would have to be evaluated. Clearly, the most appropriate storage options will be dependent on the setting and the needs of individual users.

SAFE INJECTION AND WASTE MANAGEMENT

Another probable component of home delivery of depo-subQ in Uniject is safe injection practices, including proper disposal of the used Unijects after injection. In developing countries, at least half of injections are unsafe, with providers often reusing needles and syringes repeatedly and then improperly disposing of the used syringes.^{23,26,54} Hutin et al. suggest that unsafe management of sharps waste causes 5 to 28 percent of needle stick injuries.⁵⁴ The WHO defines a safe injection as follows: "A safe injection... does not harm the recipient, does not expose the provider to any avoidable risk and does not result in any waste that is dangerous for other people."⁵⁵

As presented in the box below, institutional guidelines exist for proper syringe disposal, but would need to be adapted for use in home settings. The evidence from the literature suggests that CHWs delivering injectable contraceptives are, in many cases, able to safely and effectively dispose of their used needles, syringes, and medical supplies.^{35,37} However, disposal for a home user will likely be much more difficult and complicated.

There is limited published literature on medical waste disposal for self-injectors in developing countries. In the developed world, home-based injectors may have access to community programs for safe syringe disposal, which offer options such as:⁵⁷

- Collection of puncture-resistant containers in regular trash pick-up.
- Community drop boxes.
- Drop-off locations at biohazard sites or local medical facilities.

In the absence of such community programs, self-injectors and lay caregivers in developed-country settings may have access to mail services whereby they can send properly

Disposal of Uniject injection systems

The following proper disposal techniques are adapted from PATH's 2001 document, *Giving Safe Injections: Using Autodisable Syringes for Immunization*. Proper disposal of Uniject syringes follows standard waste disposal protocols for autodisable syringes.

- After administering the injection, the injector removes the Uniject from the skin, maintaining a firm grasp of the hard plastic.
- Immediately place the Uniject in a sturdy, leak- and puncture-proof sharps container.
- Injectors should never attempt to recap the needle.
- When three-quarters full, the sharps container should be closed, sealed, labeled and disposed of.
- Full sharps containers should optimally be incinerated; this is the preferred method as it best destroys the material and has the least environmental impact.
- Where incineration is not possible, burning sharps containers in a controlled setting is acceptable.
- Remains left after incineration or burning should be buried in a pit at least one meter deep located in a designated area for medical waste.⁵⁶

packaged sharps waste to disposal companies.⁵⁸ Such options are unlikely to be consistently available in many developing countries. For women who choose to self-inject in their own home, collecting used Unijects in a puncture-proof plastic container (e.g., a shampoo bottle) may be a feasible option. Users could then either burn the container, following proper protocols, or possibly drop it off at the home of a CHW or a local health facility. Such options would need to consider the extent to which the CHW and local health facilities are correctly managing their own sharps waste. Another factor to consider is that it may be hazardous for a user to store the low volume of sharps waste generated by one woman injecting depo-subQ quarterly at home because of the presence of children, animals, or other family members. The impact on discreet use in the home would also need to be considered. In countries where HIV and AIDS are a concern, implementation of safe injection and proper waste disposal practices in any system, including home use, is critical to limit potential disease exposure.

INFRASTRUCTURE

Proper infrastructure that can facilitate home delivery of depo-subQ in Uniject will be critical to a successful home-delivery program. At the lowest levels, home users will need access to a facility where they can acquire their depo-subQ in Uniject systems, as well as access to disposal sites for the resulting sharps waste.³⁵ At the highest levels, national governments, nongovernmental organizations, and private-sector providers who procure depo-subQ in Uniject will need to have accurate forecasting, procurement, storage, and distribution structures in place to ensure the security of this contraceptive method. These factors may need to be considered when distributing depo-subQ in Uniject in any setting.

POLITICAL SUPPORT

Based on experience introducing home delivery of DMPA IM through CBD programs, assuring that a suitable infrastructure is in place for home delivery of depo-subQ in the Uniject system will require significant support from local and national stakeholders.³⁵ New laws, guidelines, and policies may be needed for the home delivery of depo-subQ in Uniject to be successful.^{12,35,59} In many countries, paraprofessionals such as CHWs are not allowed to administer injections. Additionally, there is often considerable reluctance on the part of trained clinicians to allow paraprofessionals to administer injections.^{35,59} In order for home delivery of depo-subQ in Uniject to be acceptable, clinicians and lawmakers may need to be convinced that, not only is it acceptable for paraprofessionals

to administer injections, but that women themselves can administer subcutaneous injections using Uniject. As noted by Graham and Stanback, community distribution of injectable contraceptives is “old hat” in some regions of the world (South Asia, Central America), but is relatively new in sub-Saharan Africa.¹² However, the simplicity of Uniject may make policymakers more supportive of home administration of injectables, including self-injection, as stated by Stanback and Krueger.⁶⁰ Moving forward with home delivery of depo-subQ in Uniject may necessitate country-specific research and advocacy for improved access to family planning services and policy changes.

Conclusion and next steps

The available literature suggests that DMPA SC is a safe, reliable, and effective alternative to DMPA IM. Moreover, the subcutaneous version of DMPA offers advantages over the intramuscular formulation in that it is easier to administer and thus possesses greater potential for self-injection. The research reviewed in this document indicates that Pfizer’s DMPA SC product, depo-subQ provera 104 in the Uniject injection system, will offer new opportunities for expanding access to family planning services through home delivery, potentially including self-injection.

Based on other experiences with Uniject, a subcutaneous version of DMPA available in the injection system may accelerate and simplify non-clinic use of injectables. The availability of depo-subQ in Uniject may present an opportunity to determine how and under what conditions non-clinical family planning access can be further expanded through home and self-injection, potentially offering many women in remote, hard-to-reach areas more control over the use of their chosen family planning method. The literature suggests that self-administration of contraceptives is acceptable to users and providers alike. With subcutaneous administration being the preferred mode of injection for self-administration of a variety of medicines, the subcutaneous formulation of DMPA combined with the easy-to-use Uniject suggests this product is well suited to self-injection. Success is expected to depend on factors such as appropriate selection of users who will self-inject, targeted and adaptable training, and routine follow-up.

No information or research currently exists on best practices for training, storage, systems management, and waste disposal for self-injection of depo-subQ in Uniject. Moreover, the published product-based research on the acceptability of contraceptive self-injection does not include any formulation of DMPA. There is a need for research to assess the acceptability of self-injection

of DMPA as well as the practical considerations for implementing self-injection as another service delivery option for injectable contraceptives in lower resource settings. Research needs identified through this literature review include the following:

- Assess the acceptability of self-injection using depo-subQ in Uniject.
- Assess the training, systems, policies, and infrastructure necessary to sustainably implement a home-based delivery program for depo-subQ in Uniject, including self-injection.
- Assess storage and waste disposal requirements and options for depo-subQ in Uniject in a home setting in developing countries.

Optimally, these research needs could be met through initial, small-scale pilot studies, followed where appropriate by rigorous, large-scale operations research. In

order to provide critical information to decision-makers, PATH's *Planning for Introduction of depo-subQ provera 104™ in the Uniject™ Injection System* project plans to carry out initial research to fill some of the gaps noted above.

In collaboration with members of its global Technical Advisory Group, PATH will develop a plan to undertake qualitative research in a selected country with the aim of assessing the acceptability of depo-subQ in Uniject provided in a home setting, focusing on self-injection. Also of interest is determining best practices and assessing the needs for training, storage, waste disposal, and other practical considerations. The next steps are to define the specific research questions to be answered, identify an appropriate country in which to conduct the research, design research protocols and tools, and implement research at the country level. The project plans to begin this process in the second half of 2011.

REFERENCES

- 1 Lande R, Richey C. *Global Health Technical Brief: How Family Planning Programs Can Meet Rising Demand for Injectable Contraceptives (Based on Population Reports, Series K, No. 6)*. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health, INFO Project, Center for Communication Programs; 2006. Available at: <http://www.maqweb.org/techbriefs/tb36injectables.shtml>
- 2 United Nations, Department of Economic and Social Affairs, Population Division. *World Contraceptive Use 2007*. New York City: United Nations; 2007. Available at: http://www.un.org/esa/population/publications/contraceptive2007/contraceptive_2007_table.pdf
- 3 United Nations Population Fund. *Achieving the ICPD Goals: Reproductive Health Commodity Requirements 2000-2015*. Washington, DC: United Nations Population Fund; 2005.
- 4 Knowledge for Health (K4Health), Johns Hopkins Bloomberg School of Public Health. *Evidence-Based Synthesis: Injectables*. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health; 2009.
- 5 Moffett, J. *Improving Women's Access to Injectable Contraceptives*. Research Triangle Park, NC: Family Health International; 2009. Available at: <http://www.fhi.org/NR/rdonlyres/eriplffj3ogu25bn266kgmdace6kpme6uvhvj6jvojnspoky7pjvxiokxag4dmthylxfa4tgrwte/Mera0901.pdf>
- 6 Family Health International. *Injectable Contraceptives*. Contraceptive Technology and Reproductive Health Series. Research Triangle Park, NC: Family Health International; 2008. Available at: <http://www.fhi.org/training/en/modules/INJ/default.htm>
- 7 World Health Organization Department of Reproductive Health and Research (WHO/RHR) and Johns Hopkins Bloomberg School of Public Health / Center for Communication Programs (CCP), INFO Project. *Family Planning: A Global Handbook for Providers*. Baltimore, MD and Geneva, Switzerland: CCP and WHO; 2007. Available at: <http://info.k4health.org/globalhandbook/handbook.pdf>
- 8 World Health Organization. *Selected Practice Recommendations for Contraceptive Use 2008 Update*. Geneva, Switzerland: WHO; 2008. Available at: http://whqlibdoc.who.int/hq/2008/WHO_RHR_08.17_eng.pdf
- 9 World Health Organization. *WHO Statement on Hormonal Contraception and Bone Health*. Weekly epidemiological record. September 2005; 80(35):297-304. Available at: http://whqlibdoc.who.int/wer/WHO_WER_2005/80_297-304%28no35%29.pdf
- 10 Johns Hopkins School of Public Health. *DMPA at a Glance*. Supplement to Population Reports, New Era for Injectables, K-5, Vol. XXIII, No. 2, August 1995. Baltimore, MD: Population Information Program, Center for Communication Programs, Johns Hopkins School of Public Health; 1995. Available at: <http://info.k4health.org/pr/k5/k5dmpa.shtml>
- 11 Lande R, Richey C. *Expanding Services for Injectables: How Family Planning Programs and Providers Can Meet Clients' Needs for Injectable Contraceptives (Population Reports Series K, Number 6)*. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health, INFO Project, Center for Communication Programs; 2006. Available at: info.k4health.org/pr/k6/published/k6.pdf
- 12 Graham V, Stanback J. When opportunity comes a knockin': CBD of Depo-Provera in Africa. Presented at: Mini University, September 12, 2008; Washington, DC. Available at: <http://www.maqweb.org/miniu/presentations/When%20Opportunity%20Comes%20Knocking%20Depo.ppt>
- 13 Pfizer Inc. *depo-subQ provera 104™ medroxyprogesterone acetate injectable suspension 104 mg/0.65 mL: Physician Information*. New York, New York: Pharmacia and Upjohn Company, Division of Pfizer Inc; 2009. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=549>
- 14 Jain J, Dutton C, Nicosia A, Wajszczuk C, Bode FR, Mishell DR Jr. Pharmacokinetics, ovulation suppression and return to ovulation following a lower dose subcutaneous formulation of Depo-Provera. *Contraception*. 2004; 70(1):11-8.
- 15 Jain J, Jakimiuk AJ, Bode FR, Ross D, Kaunitz AM. Contraceptive efficacy and safety of DMPA-SC. *Contraception*. 2004; 70(4):269-75.
- 16 Toh YC, Jain J, Rahnnny MH, Bode FR, Ross D. Suppression of ovulation by a new subcutaneous depot medroxyprogesterone acetate (104 mg/0.65 mL) contraceptive formulation in Asian women. *Clinical Therapeutics*. 2004; 26(11):1845-54.
- 17 Kaunitz AM, Darney PD, Ross D, Wolter KD, Speroff L. Subcutaneous DMPA vs. intramuscular DMPA: A 2-year randomized study of contraceptive efficacy and bone mineral density. *Contraception*. 2009; 80(1):7-17.
- 18 Simon MA, Shulman LP. Subcutaneous versus intramuscular depot methoxyprogesterone acetate: a comparative review. *Women's Health*. 2006; 2(2):191-7.
- 19 Arias RD, Jain JK, Brucker C, Ross D, Ray A. Changes in bleeding patterns with depot medroxyprogesterone acetate subcutaneous injection 104 mg. *Contraception*. 2006; 74(3):234-8.
- 20 Prettyman J. Subcutaneous or intramuscular? Confronting a parenteral administration dilemma. *Medsurg Nursing*. 2005; 14(2):93-8.
- 21 Arias RD, Nelson AL, Petta CA. A New era in injectable contraceptive care. PowerPoint presentation. Symposium. No date.
- 22 PATH. *The Uniject Device*. Seattle: PATH; 2009.
- 23 Safe injection page. PATH website. Available at: <http://www.path.org/safe-injection.php>. Accessed on April 22, 2010.

- 24 Bahamondes L, Marchi NM, Cristofolletti MdL, et al. Uniject as a delivery system for the once-a-month injectable contraceptive Cyclofem in Brazil. *Contraception*. 1996; 53(2):115-9.
- 25 Sutanto A, Suarnawa IM, Nelson CM, Stewart T, Soewarso TI. Home delivery of heat-stable vaccines in Indonesia: outreach immunization with a prefilled, single-use injection device. Geneva, Switzerland: World Health Organization; 1999. Available at: [http://www.who.int/bulletin/archives/77\(2\)119.pdf](http://www.who.int/bulletin/archives/77(2)119.pdf).
- 26 Tsu VD, Sutanto A, Vaidya K, Coffey P, Widjaya A. Oxytocin in prefilled Uniject injection devices for managing third-stage labor in Indonesia. *International Journal of Gynecology and Obstetrics*. 2003; 83(1):103-11.
- 27 Levin CE, Nelson CM, Widjaya A, Moniaga V, Anwar C. The costs of home delivery of a birth dose of hepatitis B vaccine in a prefilled syringe in Indonesia. *Bulletin of the World Health Organization*. 2005; 83(6):456-61.
- 28 Fernandez V, Montufar E, Ottolenghi E, Enge K. *Injectable Contraceptive Service Delivery Provided by Volunteer Community Promoters*. Guatemala City: Population Council project report, 1997.
- 29 Katz KR, West CG, Doumbia F, et al. *Increasing Access to Family Planning Services in Rural Mali Through CBD*. International Family Planning Perspectives. 1998; 24(3).
- 30 Oxford Policy Management. *External Evaluation of the Lady Health Worker Programme*. 2009 http://www.opml.co.uk/policy_areas/statistics/quantitative_information_for_policy_and_programme/6241_lhw.html
- 31 Quiroga R, Halkyer P, Gil F, Nelson C, Kristensen D. A prefilled injection device for outreach tetanus immunization by Bolivian traditional birth attendants. *Rev Panam Salud Publica* 1998; 4:20-25.
- 32 PATH, World Health Organization. *Time and Motion Study with Potential Human Papilloma Virus (HPV) Vaccine Product Presentations*. October 2009.
- 33 Hudgins, A and Dowling, P. *Comparative Analysis of Supply Chain Characteristics of depo-subQ provera 104™ in the Uniject® Device and DMPA IM*. John Snow Inc: April 2010.
- 34 Muller N. *Waste Management Analysis of depo-subQ in Uniject Systems Compared to DMPA Intramuscular Vial and Syringe*. Seattle: PATH; 2010.
- 35 Weil B, Krueger K, Stanback J, Hatzell Hoke T. *Provision of Injectable Contraception Services through CBD: An Implementation Handbook*. Raleigh, NC: Family Health International; 2008. Available at: http://www.fhi.org/en/rh/pubs/booksreports/cbd_dmpa_imp.htm
- 36 Family Health International. *Best Practices in CBD Programs in sub-Saharan Africa: Lessons Learned from Research and Evaluation*. Frontiers in Reproductive Health Program (FRONTIERS), FHI, Advance Africa. Washington, DC: FHI; December 2, 2002. Available at: http://www.popcouncil.org/pdfs/frontiers/CBD_seminar.pdf
- 37 Stanback J, Mbonye A, LeMelle J, Bekiita M, Ssekito, G, Kajura NJ. *Final Report: Safety and Feasibility of CBD of Depo Provera in Nakasongola, Uganda*. Kampala, Uganda: Family Health International/Save the Children USA; 2005. Available at: <http://www.fhi.org/NR/rdonlyres/edzlc2z6pk4rx7iwcwmkzezyvtyqfbqarnqx45z2sovww7maxikndkkvww6sxklesstvajuxqwz2w4xb/CBDDepoFinalReportenrh.pdf>
- 38 Khuda B, Kane TT, Phillips JF, eds. *Improving the Bangladesh Health and Family Planning Programme: Lessons Learned through Operations Research*. Dhaka, Bangladesh: International Centre for Diarrhoeal Disease Research, Bangladesh; 1997. Available at: <http://dSPACE.icddr.org/dSPACE/bitstream/123456789/2563/1/Improving+the+bangladesh+health+and+family+planning+programme,+monograph+5.pdf>
- 39 World Health Organization. *The Global Shortage of Health Workers and its Impact: Factsheet No. 302*. Geneva, Switzerland: WHO; 2006.
- 40 Family Health International. *Community-Based Health Workers Can Safely and Effectively Administer Injectable Contraceptives: Conclusions from a Technical Consultation*. Research Triangle Park, NC: FHI; 2009. Available at: http://www.who.int/reproductivehealth/publications/family_planning/WHO_CBD_brief/en/index.html
- 41 Livermore P. Teaching home administration of sub-cutaneous methotrexate. *Paediatric Nursing*. 2003; 15(3):28-32.
- 42 Israel F, Reymond L, Slade G, Menadue S, Charles MA. Lay caregivers' perspectives on injecting subcutaneous medications at home. *International Journal of Palliative Nursing*. 2008; 14(8):390-5.
- 43 Bevan JS, Newell-Price J, Wass JAH, et al. Home administration of lanreotide Autogel by patients with acromegaly, or their partners, is safe and effective. *Clinical Endocrinology*. 2008; 68(3):343-9.
- 44 Jakimiuk A. A new highly effective subcutaneous contraceptive injection. Presented at: 7th European Society of Contraception Congress, Genoa, Italy, Department of Surgical Gynecology, University School of Medicine, Lublin, Poland. April 10, 2002.
- 45 Bahamondes L, Marchi NM, Nakagava HM, et al. Self-administration with Uniject of the once-a-month injectable Cyclofem. *Contraception*. 1997; 56(5):301-4.
- 46 Stanwood NL, Eastwood K, Carletta A. Self-injection of monthly combined hormonal contraceptive. *Contraception*. 2006; 73(1):53-5.
- 47 Prabhakaran S. Self-administration of injectable contraceptives. *Contraception*. 2008; 77(5):315-7.
- 48 Lakha F, Henderson C, Glasier A. The acceptability of self-administration of subcutaneous Depo-Provera. *Contraception*. 2005; 72(1): 14-18.
- 49 Somkuti SC, Schertz JC, Moore M, Ferrande L, Kelly E, Gonal-F Prefilled Pen in OI Study 24785 Group. Patient experience with follitropin alfa prefilled pen versus previously used injectable gonadotropins for ovulation induction in oligoanovulatory women. *Current Medical Research and Opinion*. 2006; 22(10): 1981-1996. 2006; 22(10):1981-96.
- 50 Ott MJ. "I want to do it myself!" Interferon self-injection for children with chronic viral hepatitis. *Gastroenterology Nursing*. 2005; 28(5):406-9.
- 51 Muller, N. *Uniject Global Training Experience*. PATH internal document: 2010.
- 52 Pfizer Inc. *DEPO-PROVERA® Contraceptive Injection medroxyprogesterone acetate injectable suspension, USP: Physician Information*. New York, New York: Pharmacia and Upjohn Company, Division of Pfizer Inc; 2006. Available at: http://www.pfizer.com/files/products/ppi_depo_provera_contraceptive.pdf
- 53 Solter C. *Module 6: DMPA Injectable Contraceptive: Comprehensive Reproductive Health and Family Planning Training Curriculum*. Watertown, MA: Medical Services Unit, Pathfinder International; 1999. Available at: http://www.pathfind.org/pf/pubs/module_6.pdf
- 54 Hutin Y, Hauri A, Chiarello L, Catlin M, et al. *Best Infection Control Practices for Intradermal, Subcutaneous, and Intramuscular Needle Injections*. Geneva, Switzerland: World Health Organization; 2003. Available at: <http://www.who.int/bulletin/volumes/81/7/Hutin0703.pdf>
- 55 World Health Organization. *Revised Injection Safety Assessment Tool (Tool C-Revised)*. Geneva, Switzerland: WHO; 2008. Available at: http://www.who.int/injection_safety/Injection_safety_final-web.pdf
- 56 PATH. *Giving Safe Injections: Using Autodisable Syringes for Immunization*. Seattle, WA: PATH; 2001. Available at: <http://www.path.org/publications/detail.php?i=474>
- 57 Macalino GE, Springer KW, Rahman ZS, Vlahov D, Jones TS. Community-based programs for safe disposal of used needles and syringes. *Journal of Acquired Immune deficiency Syndromes and Human Retrovirology*. 1998; 18 Suppl 1:S111-9.
- 58 At-home sharps disposal causes concern. *Home Healthcare Nurse*. 2003; 21(11):722-3.
- 59 Richardson F, Chirwa M, Fahnestock M, Bishop M, Emmart P, and McHenry B. *CBD of Injectable Contraceptives in Malawi*. Washington, DC: Futures Group International, Health Policy Initiative, Task Order 1; 2009. Available at: http://www.healthpolicyinitiative.com/Publications/Documents/754_1_Community_based_Distribution_of_Injectable_Contraceptives_in_Malawi_FINAL.pdf
- 60 Stanback J, Kreuger K. Re: Self-administration of injectable contraceptives. Letters to the Editor. *Contraception*. 2008; 78:513-514.

About depo-subQ in the Uniject injection system

A new formulation and presentation of the contraceptive depot medroxyprogesterone acetate (DMPA) for subcutaneous administration in a prefilled injection system, known as depo-subQ provera 104™ in the Uniject™ injection system (depo-subQ in Uniject), will soon be available to women in developing countries. The contraceptive will be prepackaged with a single dose inside Uniject, an autodisable syringe developed by PATH. Due to its ease of administration and likely high acceptability among women seeking contraception options, introduction of depo-subQ in Uniject provides opportunities to both strengthen clinic injection services and extend injectable contraceptive delivery safely and effectively beyond the clinic, such as through home delivery. The product is also expected to have advantages for supply chain management. The product will be marketed by Pfizer, and PATH is leading global planning for its introduction.

Uniject is a trademark of BD.



PATH is an international nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being.

MAILING ADDRESS
PO Box 900922
Seattle, WA 98109 USA

info@path.org
www.path.org

STREET ADDRESS
2201 Westlake Avenue
Suite 200
Seattle, WA 98121 USA

July 2011