



Isotretinoin Pregnancy Risk Management Program

Presented by:

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Objectives:

- Walkthrough and Demonstration of Program Steps
- Program Enhancements
- Call Center Data

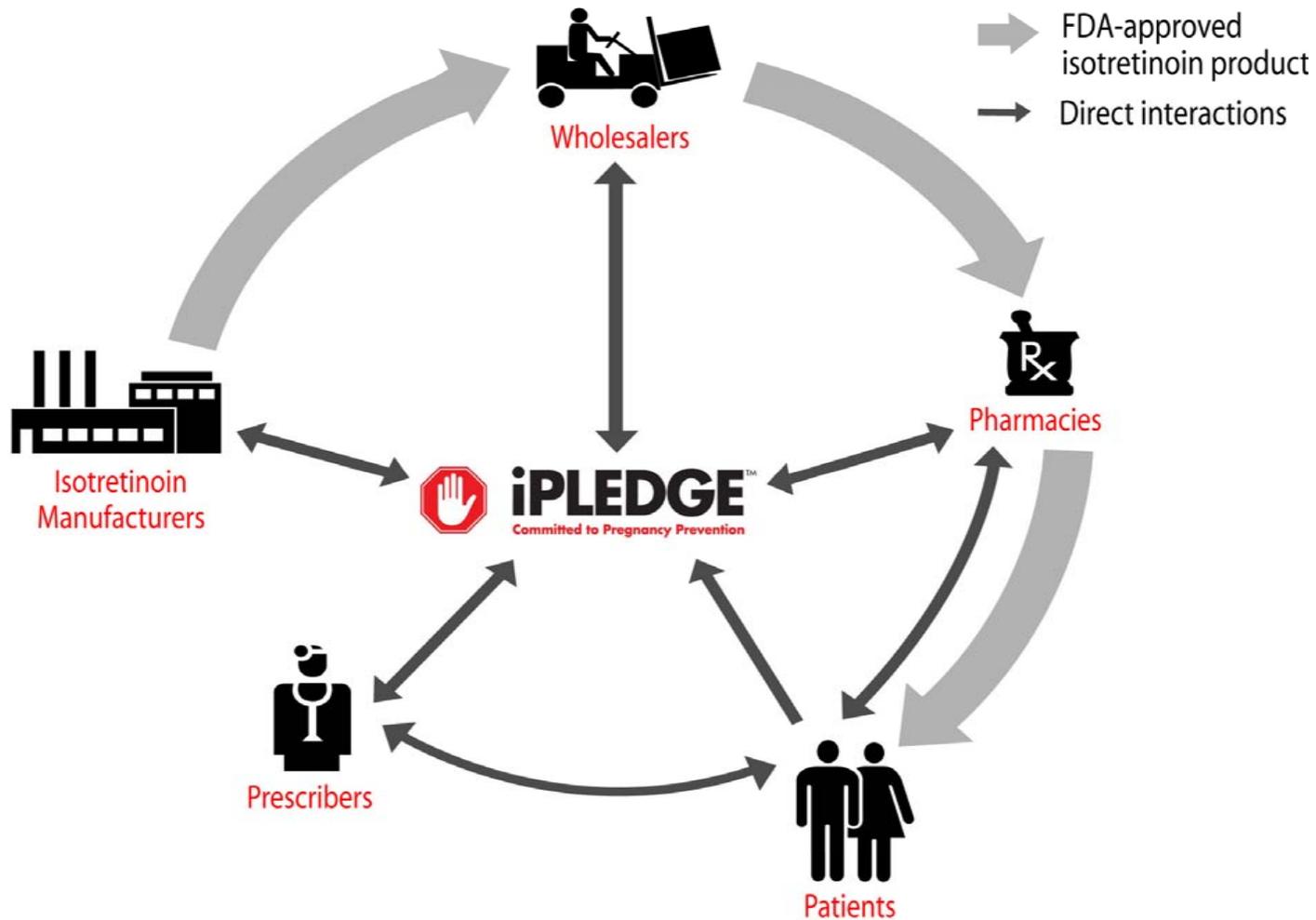
Walkthrough and Demonstration of Program Steps

Isotretinoin Public Health Goal

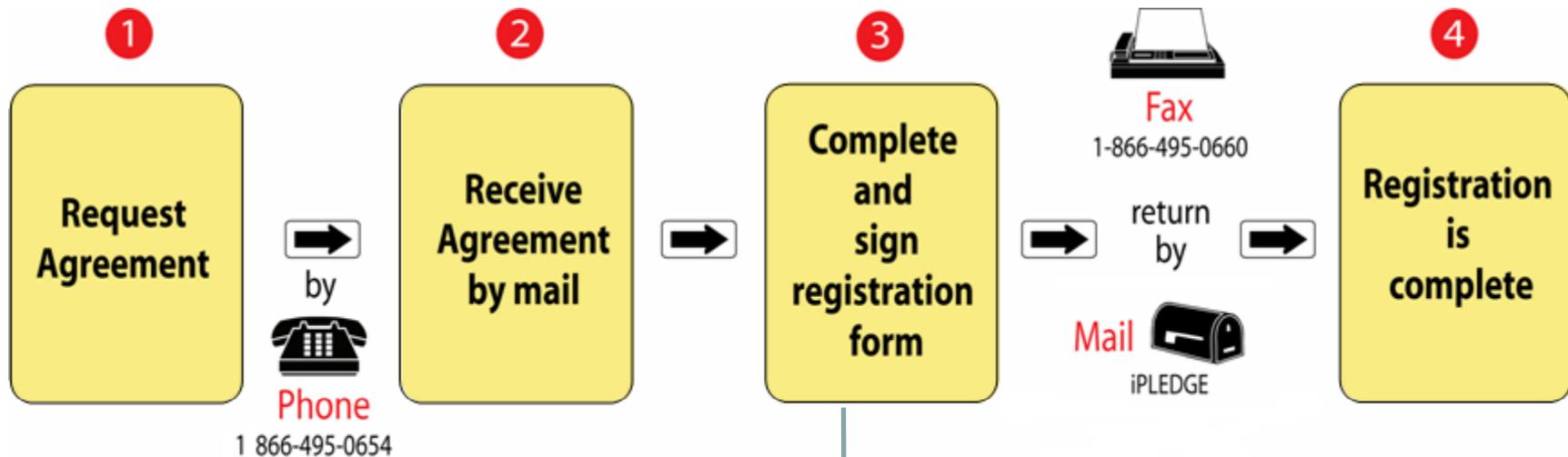
To eliminate fetal exposure to isotretinoin by ensuring that:

- No female patient starts isotretinoin therapy if pregnant
- No female patient on isotretinoin therapy becomes pregnant

Who Is Part of iPLEDGE?

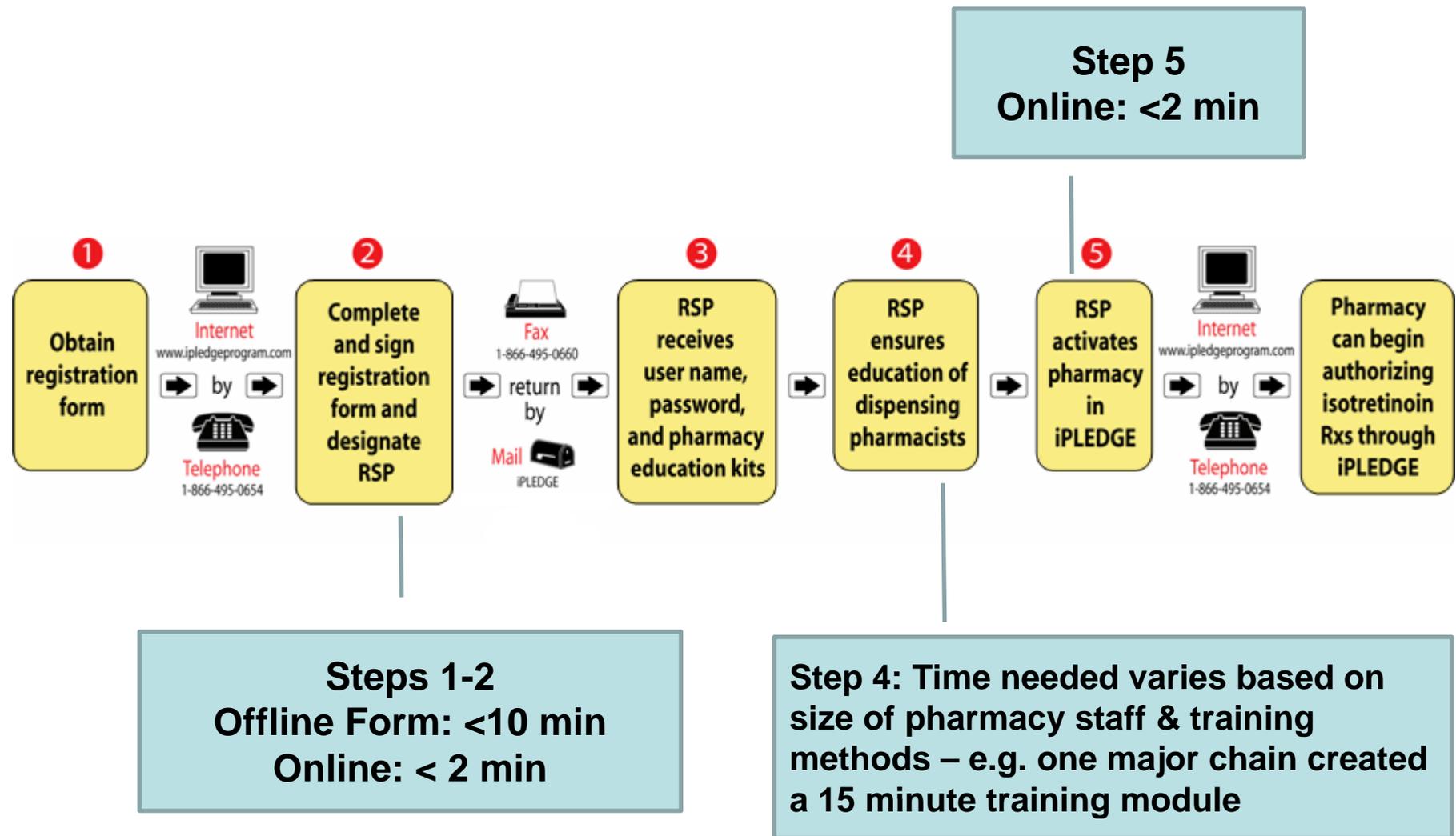


Wholesaler Registration



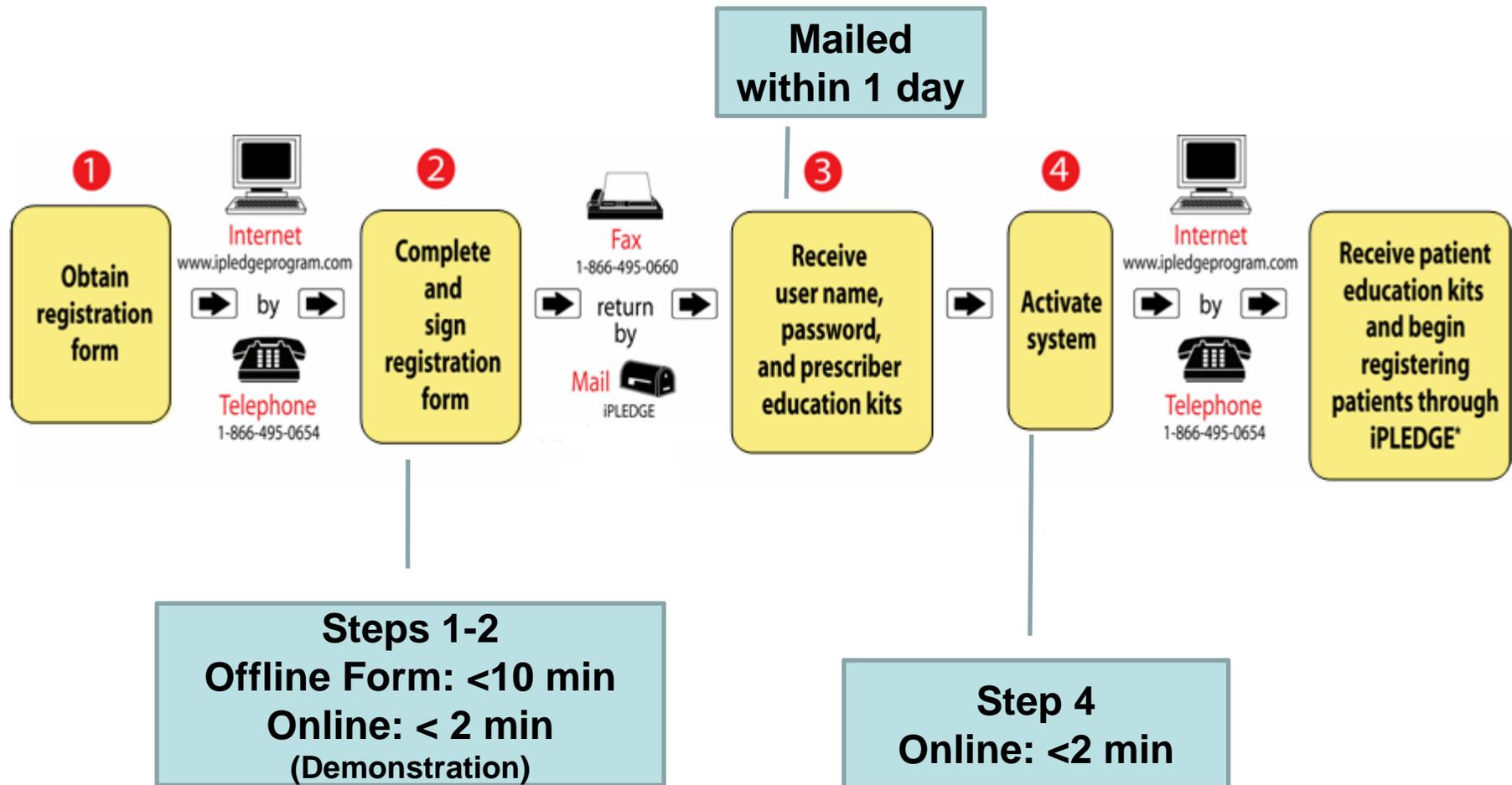
Minimal Time required by wholesaler; < 1 hour

Pharmacy Registration and Activation



RSP = responsible site pharmacist

Prescriber Registration and Activation



Expedited registration kits can be requested through the iPLEDGE Call Center

iPLEDGE Registrations and Activations

Stakeholder	Total Registered & Activated at the end of:		
	Year 3	Year 4	Year 5
Retail Pharmacies	43,477	44,962	43,064
Prescribers (written at least 1 prescription)	14,620	14,938	14,444
Wholesalers	184	181	183

Year 3: Mar 1, 2008 – Feb 28, 2009

Year 4: Mar 1, 2009 – Feb 28, 2010

Year 5: Mar 1, 2010 – Feb 28, 2011

Demonstration

Prescriber Registration

Prescriber Registration

Release 4.3.1 Environment

Patient Path: Females of Childbearing Potential

Potential
Patient
for
Isotretinoin

Patient Path: Females of Childbearing Potential

Mandatory 30-day wait

iPLEDGE



Pt. ID #

Potential
Patient
for
Isotretinoin

Initial Registration Visit:

- Determine if childbearing potential
- Screening pregnancy test
- Informed consent
- Prescriber educates and registers patient (iPLEDGE educational kit including iPLEDGE ID card)
- Enter patient demographics
- System enforced 30-day wait before 1st Rx

Patient Visit duration:
varies by practice

Online registration:
< 3 min

iPLEDGE Cumulative Patient Registrations

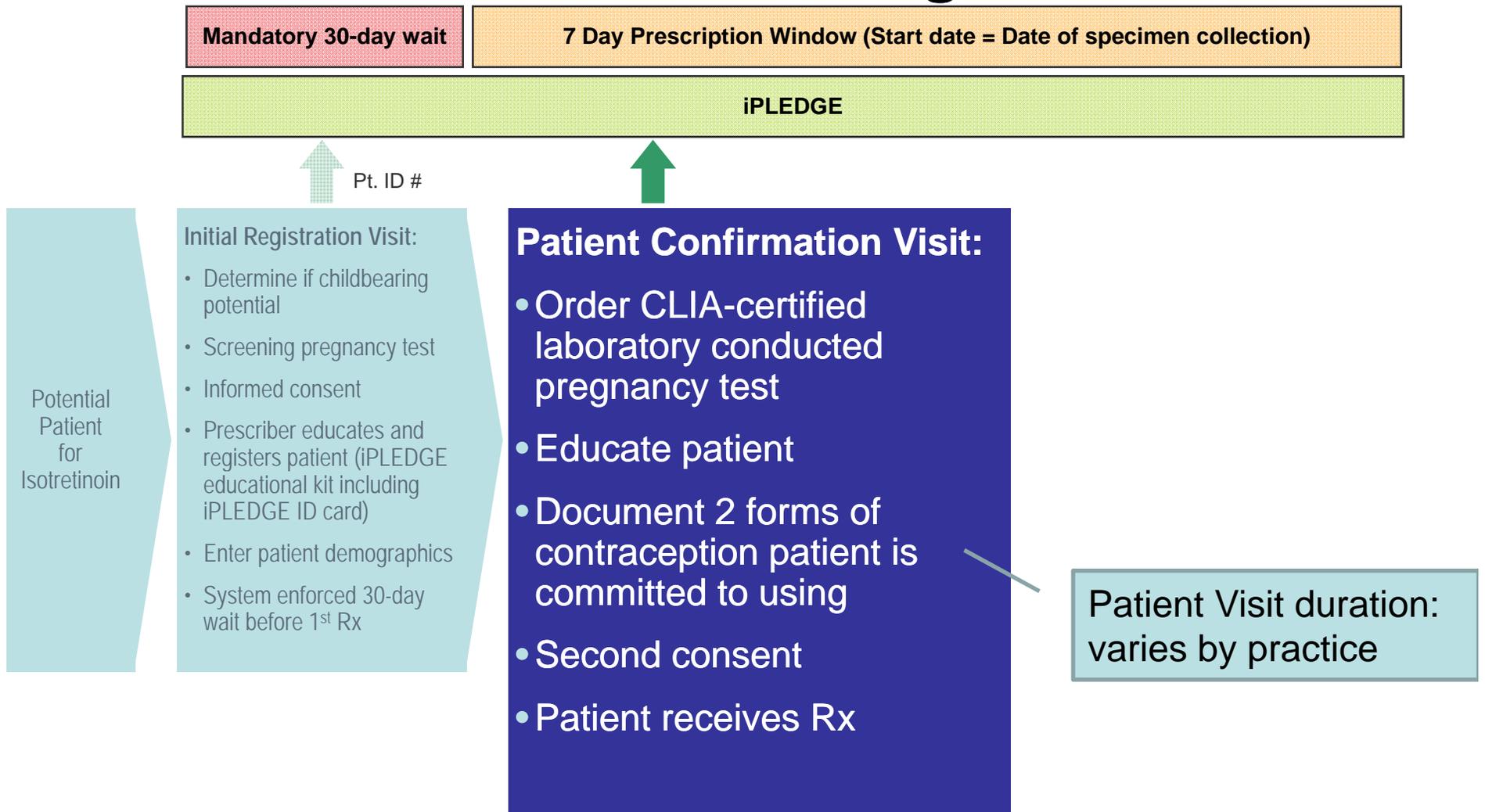
Patient Type	Total Registered at the end of:		
	Year 3	Year 4	Year 5
FCBP	362,023	477,948	569,385
FNCBP	31,626	39,358	45,484
Male	396,237	521,191	620,012
Total	789,886	1,038,497	1,234,881

Year 3: Mar 1, 2008 – Feb 28, 2009

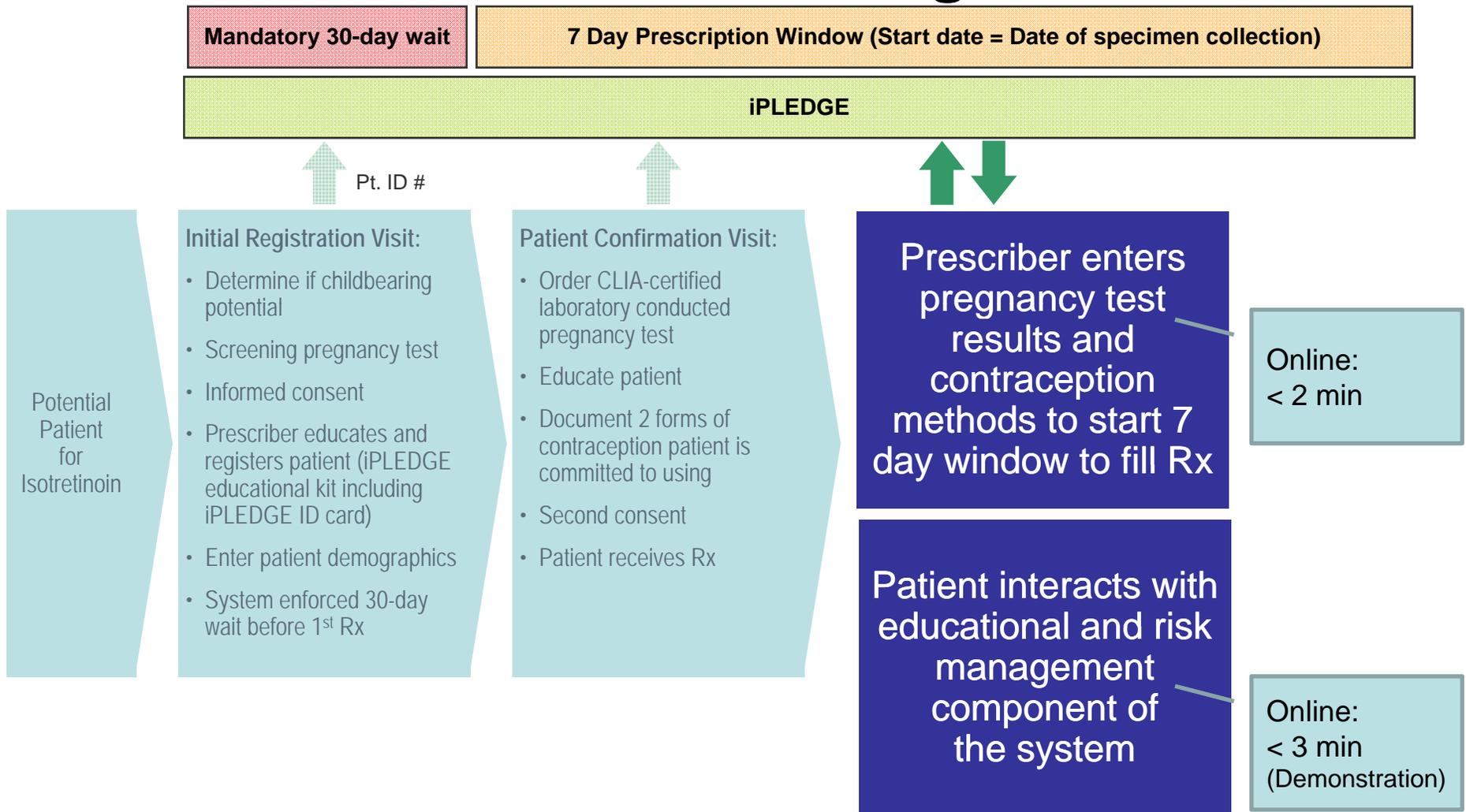
Year 4: Mar 1, 2009 – Feb 28, 2010

Year 5: Mar 1, 2010 – Feb 28, 2011

Patient Path: Females of Childbearing Potential



Patient Path: Females of Childbearing Potential



Demonstration

FCBP Patient Demonstrates Comprehension

FCBP Patient Demonstrates Comprehension

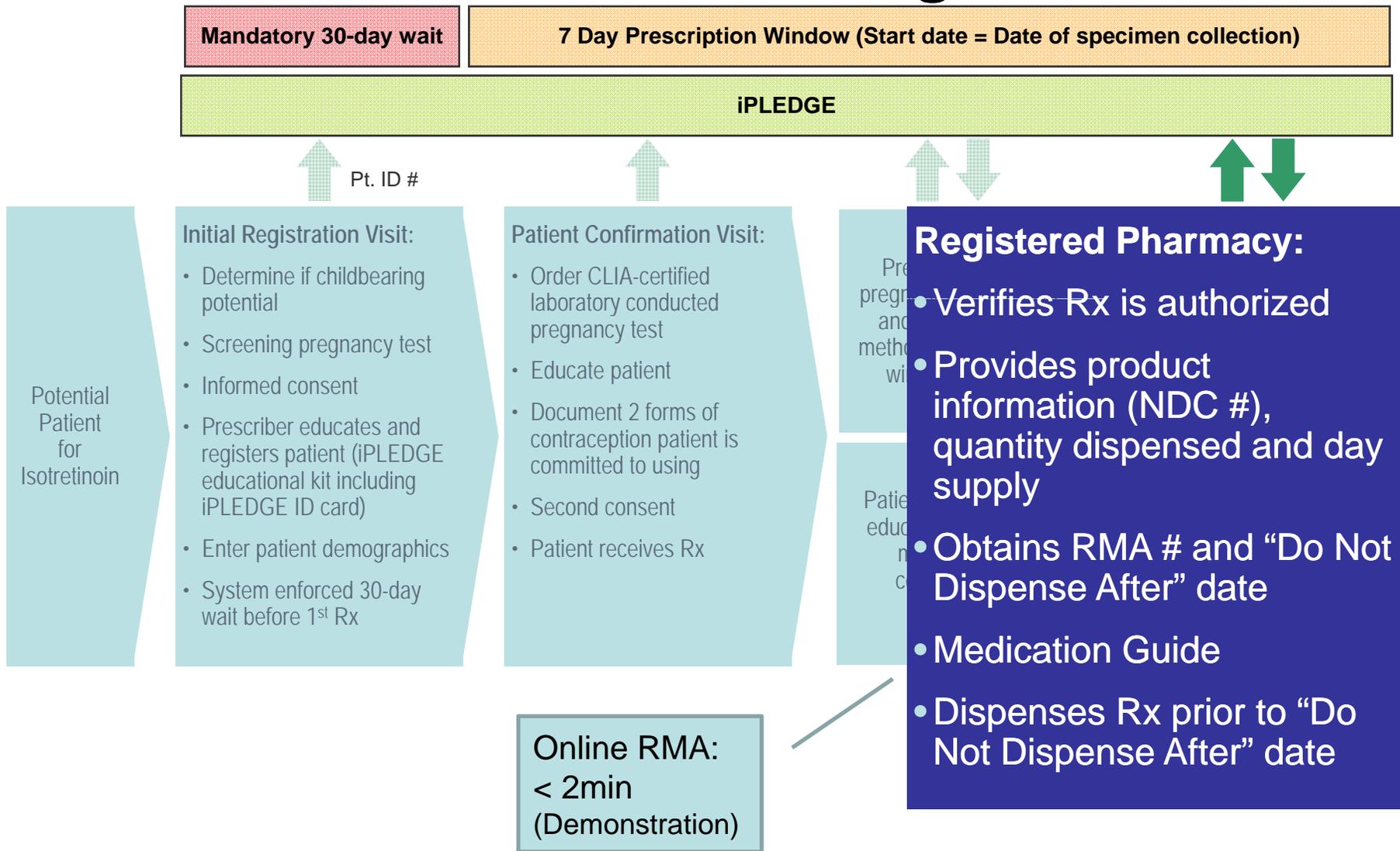
Release 4.3.1 Environment

Monthly Comprehension Testing for FCBP

Monthly Comprehension Testing for FCBP about the Use of Contraception and the Risk of Birth Defects						
iPLEDGE Year	Year 3		Year 4		Year 5	
	Non-pregnant	Pregnant	Non-pregnant	Pregnant	Non-pregnant	Pregnant
	N=168,377 N(%)	N=175 N(%)	N=181,899 N(%)	N=179 N(%)	N=162,743 N(%)	N=154 N(%)
Passed first time	157,634 (93.62)	160 (91.42)	170,748 (93.87)	170 (94.97)	153,132 (94.09)	143 (92.86)

Not all non-pregnant patients answered the required monthly questions. Some patients counted as Year 5 patients did not answer the required monthly questions for several reasons. For example, a patient that was registered on February 15, 2011 was considered a Year 5 patient, but she could not have been confirmed the first time until March 16, 2011 and would not have answered her questions during Year 5. Some patients may have more than one course of treatment represented in the data.

Patient Path: Females of Childbearing Potential



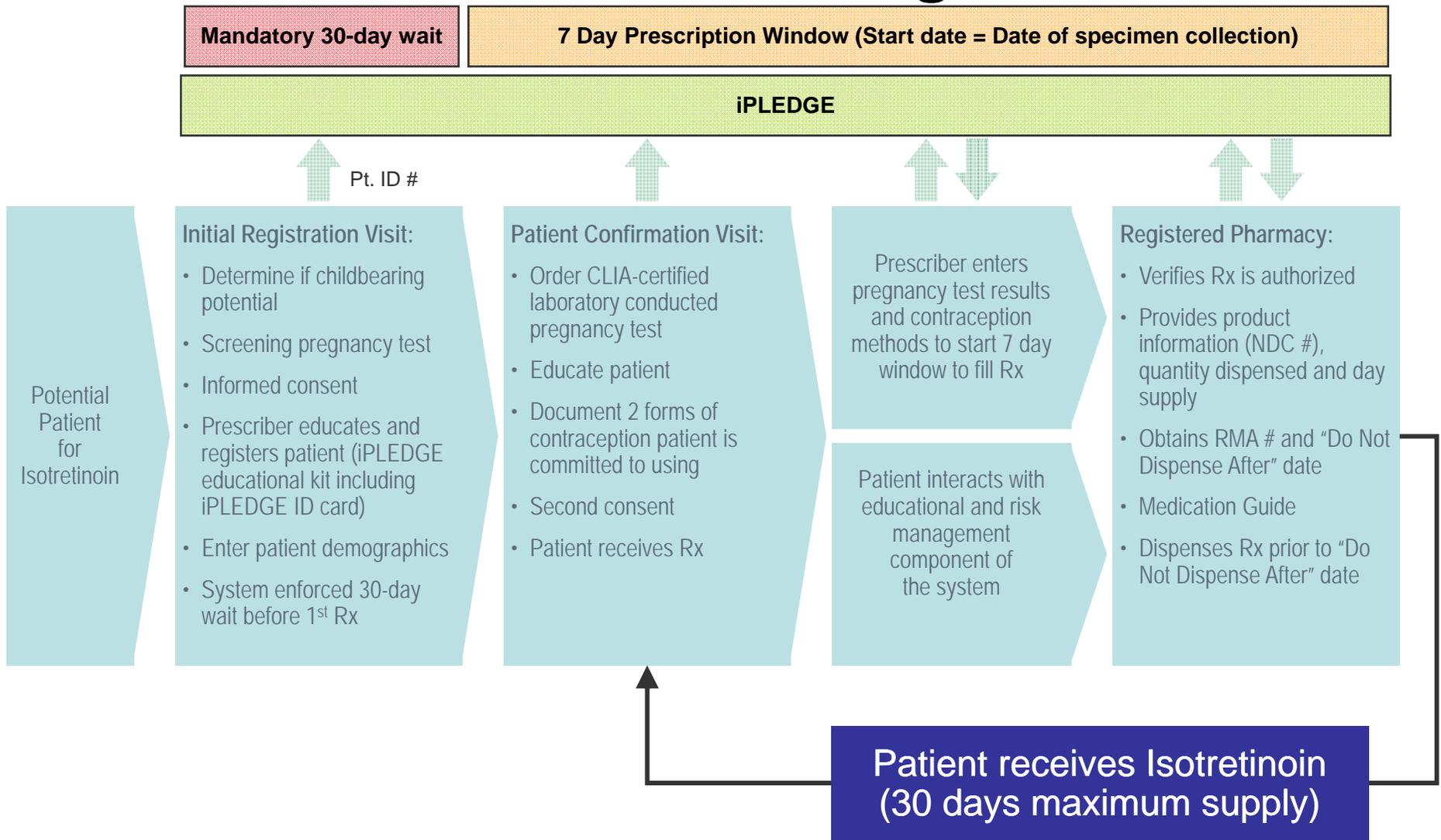
Demonstration

Pharmacy Fills Prescription

Pharmacy fills Prescription

Release 4.3.1 Environment

Patient Path: Females of Childbearing Potential



After Isotretinoin Therapy

- Must continue to use 2 forms of contraception for 30 days after the last dose of isotretinoin
- Obtain laboratory pregnancy tests:
 - immediately after the last dose of isotretinoin
 - 30 days after the last dose of isotretinoin
- Prescriber must enter both post-therapy pregnancy test results in the iPLEDGE system

Patient Path: Males & Females of Non Childbearing Potential

30 Day Prescription Window (Start Date = Date of Office Visit)

iPLEDGE

↑ Pt. ID #

↑ ↓

Potential Patient for Isotretinoin

- Determine if childbearing potential
- Informed consent
- Prescriber educates and registers patient (iPLEDGE educational kit including iPLEDGE ID card)
- Enter patient demographics
- Prescriber confirms patient

Registered Pharmacy:

- Verifies Rx is authorized
- Provides product information (NDC #), quantity dispensed and day supply
- Obtains RMA # and "Do Not Dispense After" date
- Medication Guide
- Dispenses Rx prior to "Do Not Dispense After" date

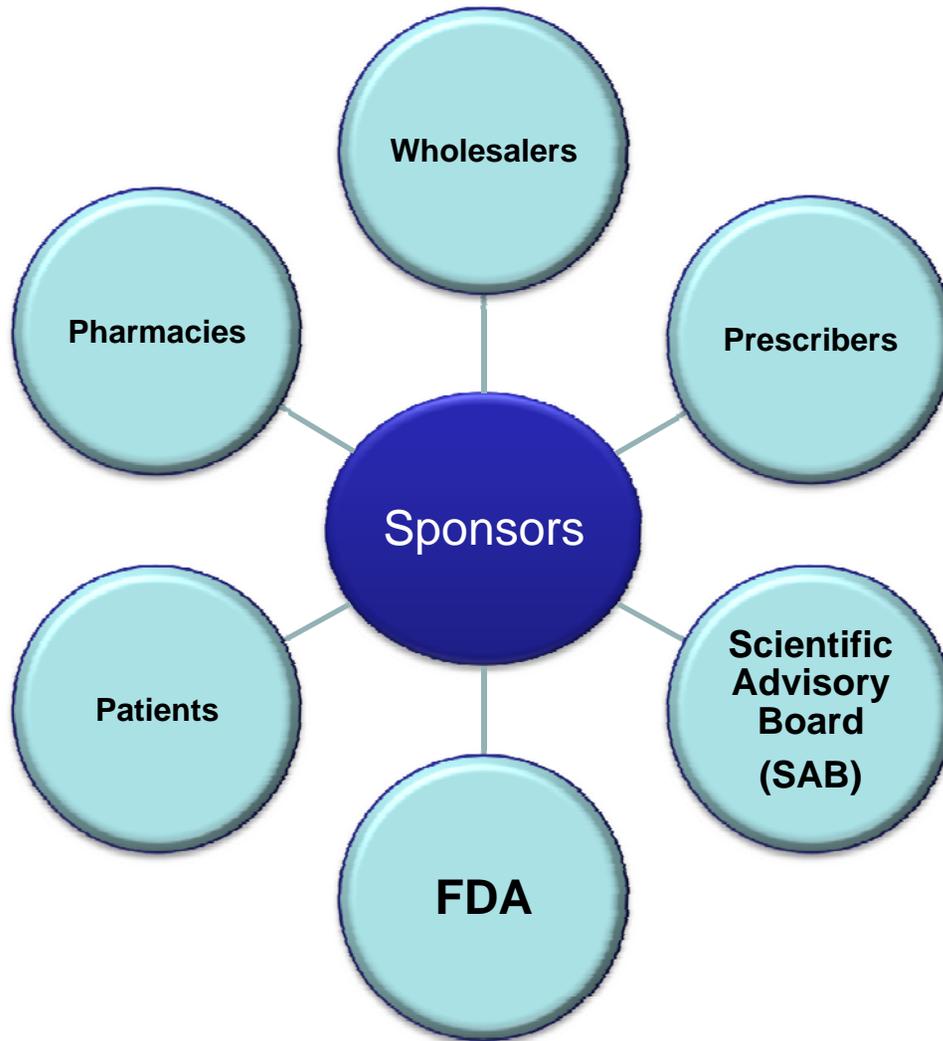
Patient Visit duration: varies by practice but shorter than FCBP visit

Online registration: < 3 min

Patient receives Isotretinoin (30 days maximum supply)

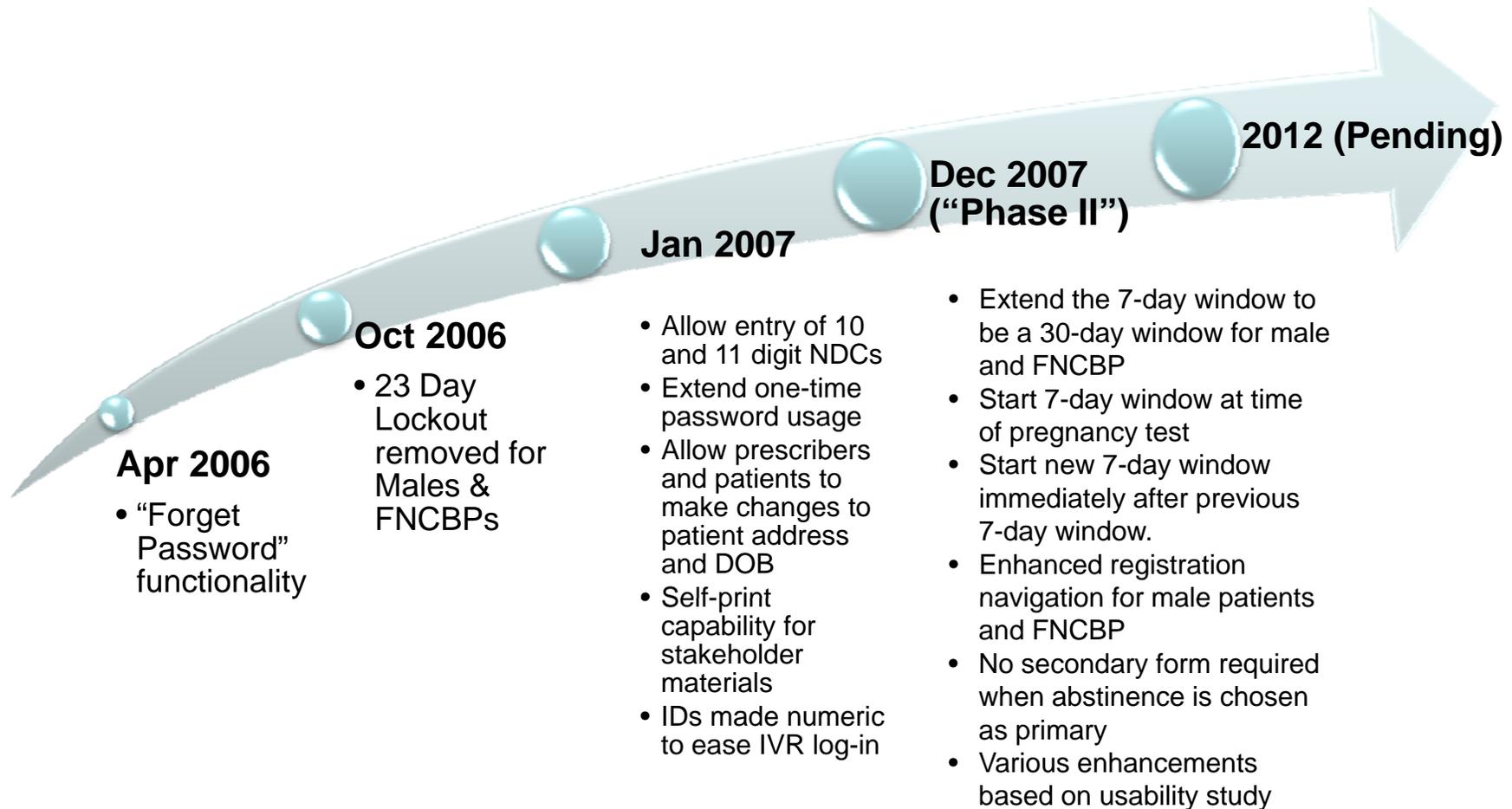
Program Enhancements

Program Enhancements



- Since the launch of the iPLEDGE program in March of 2006 there has been continuous evaluation and periodic enhancement of the program.
- All feedback received from stakeholders is considered.

History of Enhancements



2012 Pending Enhancements

Prescribers & Designees

- Request information on previous prescription window (no RMA recorded)
- Automatic Categorization of Female Patients (through a “wizard”)
- Additional prescriber attestation points & Designee attestation
- Qualitative serum pregnancy test
- Re-registration of existing patients
- Change patient risk category
- Correcting contraception choices
- Various reminders & enhanced descriptions

Patients

- Request information on previous prescription window (no fill recorded)
- Reminder regarding abstinence as birth control method
- “For Patients” button on homepage

Pharmacies

- Visibility of Risk Management Authorization (RMA) number
- Display List of Risk Management Authorization (RMA) numbers
- 12-digit RMA and check digit for optional use in pharmacy management systems
- RMA Denial Message

Prescriptions dispensed without RMA

	Year 3	Year 4	Year 5
Confirmed incidents of dispensing without an RMA	1,169	1,109	932
Total number of prescriptions authorized	1,114,421	1,179,274	1,006,079

- No systematic method in iPLEDGE to detect if a pharmacy dispenses without a Risk Management Authorization (RMA). Typically only discovered if reported by a stakeholder.
- A planned enhancement seeks to address this by checking the outcome of the previous prescription:
 - When the system sees that a RMA was not obtained, the prescriber and patient will be queried at their next interaction on whether the previous prescription was filled. If yes, they are asked to provide the name of the Pharmacy that dispensed the drug

Demonstration

Request Pharmacy Fill Information
(Enhancement)

Prescriber confirms FCBP
System has no record of a Rx Fill in previous window

Release 4.3.1 Environment

FCBP Misclassified as FNCBP

- The iPLEDGE Program has specific criteria for female patients to be classified as a Female of Non Childbearing Potential patient
- Prescribers have been found to misclassify FCBP patients as FNCBP due to misinterpretation of the requirements
- The program initiated campaigns targeting prescribers who had a higher than average ratio of FNCBP to FCBP
 - Educated prescribers on the iPLEDGE criteria for FNCBP risk categorization
 - Requested prescribers to review a list of their FNCBP patients and respond with the reason for FNCBP categorization for each. (A request for reclassification of a patient to FCBP was accepted, when appropriate.)

Campaign Year	# of Prescribers	# of Patients	# of Patient that Met an FNCBP Criterion	# of Patients that did not meet an FNCBP Criterion	% of Patients Requiring Re-classification
2007	198	616	469	147	23.86
2009	300	1,579	1,015	564	35.72
2010	174	817	569	248	30.35

FCBP Misclassified as FNCBP

- A pending enhancement will reduce misinterpretation of program requirements and make it easier for prescribers to comply with iPLEDGE requirements regarding patient risk category:
 - Categorization of new patients will be “wizard”-driven. The system will assist in assigning a patient to the proper risk category using a series of Yes/No questions as follows:
 - Has patient had a hysterectomy?
 - Has patient had a bilateral oophorectomy?
 - Is this patient post-menopausal?
 - System will classify the patient based on the system input
 - Prescribers may request an exception if an unusual medical circumstance exists

Demonstration

Prescriber Registers FNCPB
(Enhancement)

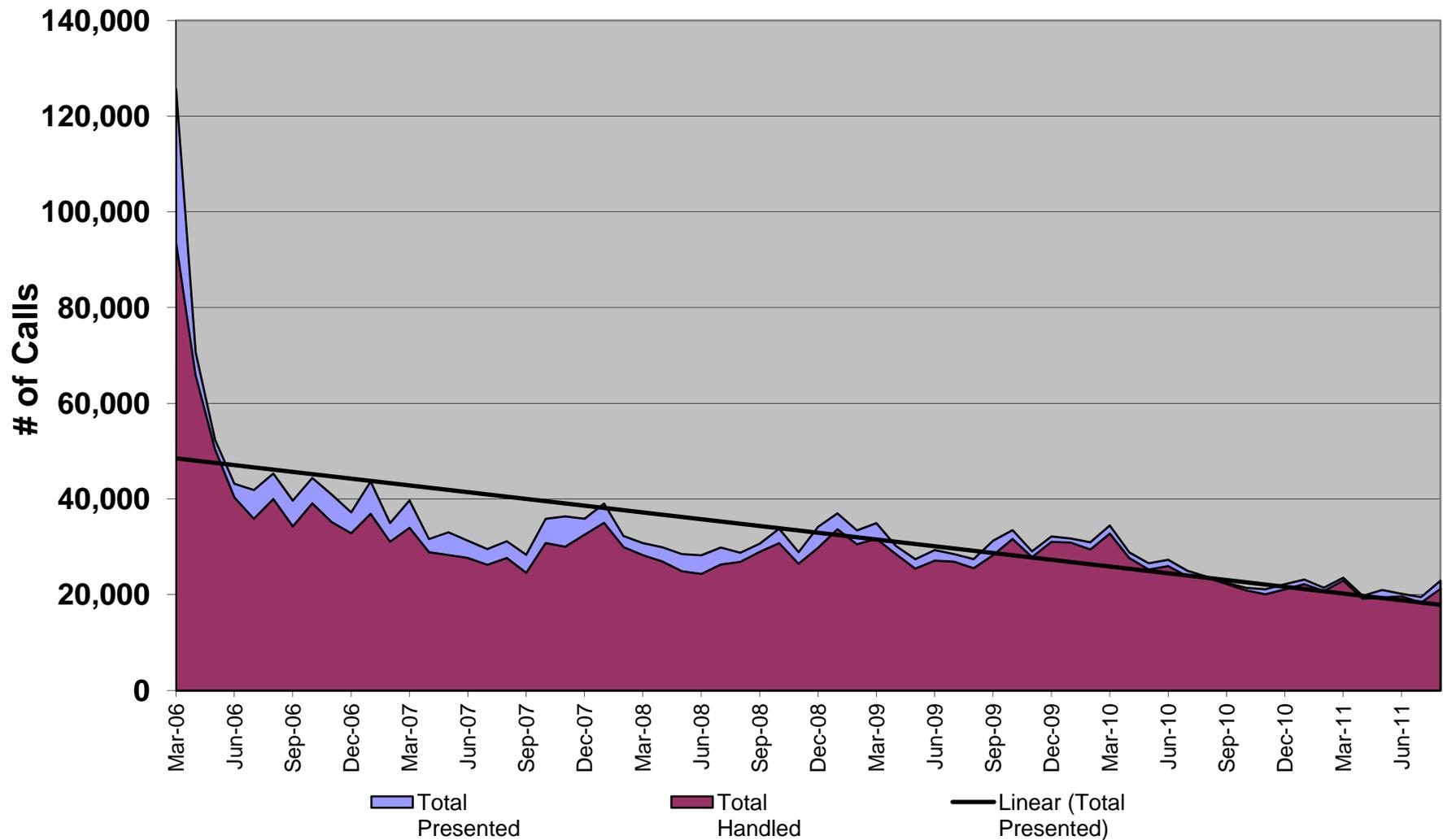
Prescriber registers FCBP (system determines patient type)

Release 4.3.1 Environment

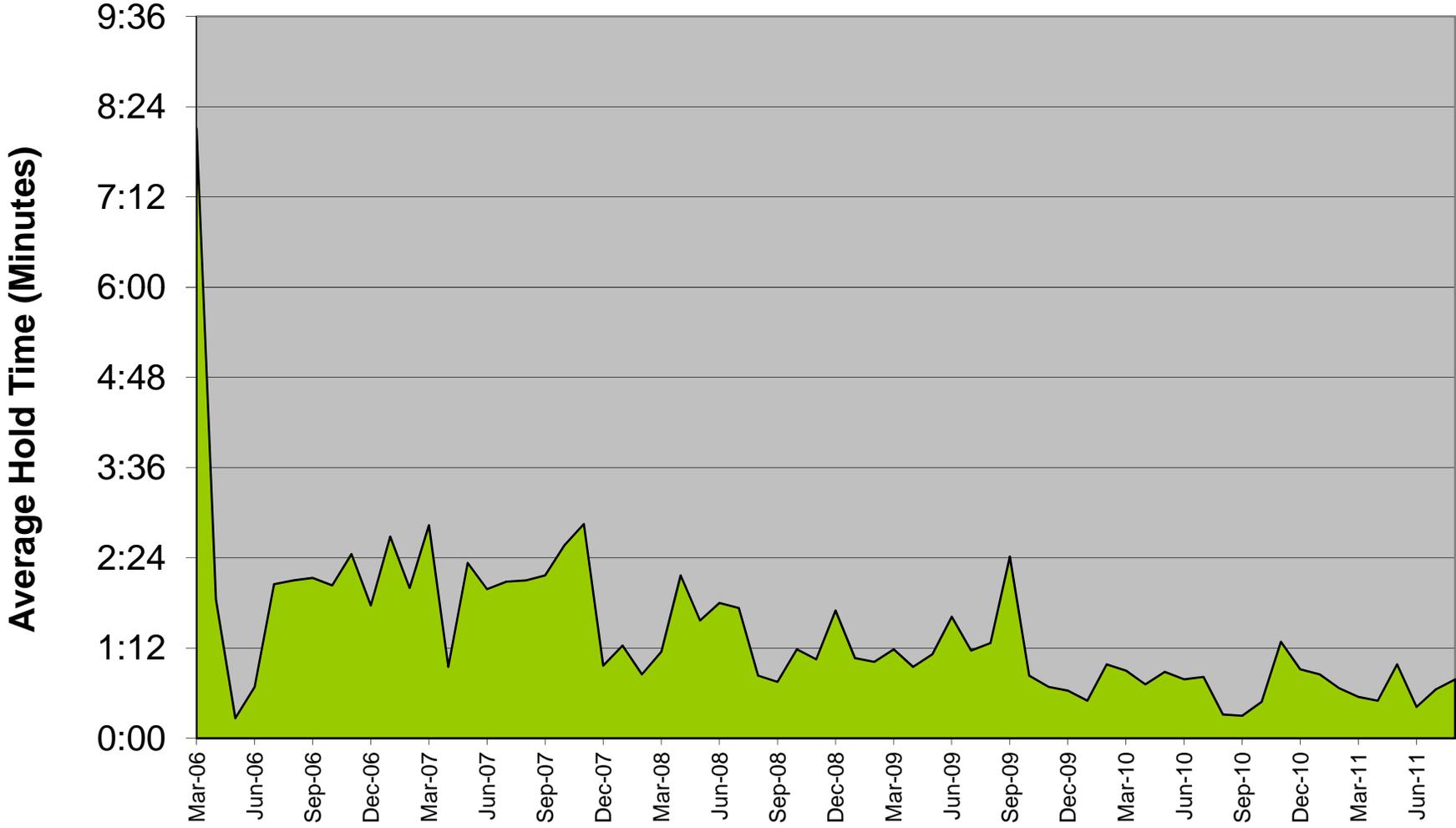
Call Center Data

iPLEDGE Call Center Volumes

(Mar 2006 - Aug 2011)

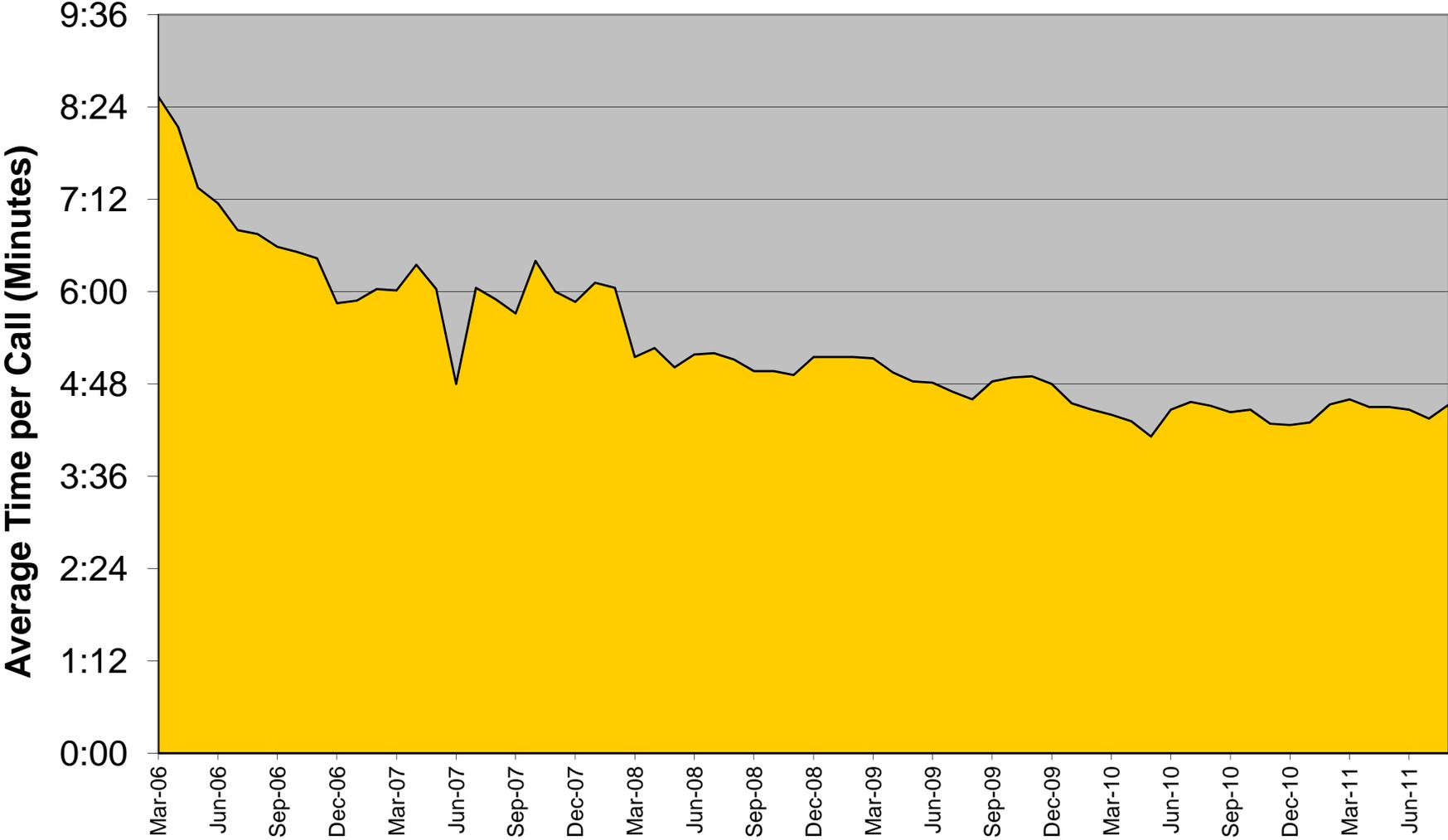


iPLEDGE Call Center Average Hold Time (Tier 1)



iPLEDGE Call Center

Average Time per Call (Tier 1)





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Isotretinoin Pregnancy Risk Management Program

Pregnancy Data

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iPLEDGE Pregnancies by Isotretinoin Exposure

Isotretinoin Exposure	Year 3 (N = 190) N (%)	Year 4 (N = 186) N (%)	Year 5 (N = 155) N (%)
Exposed	183 (96.3)	176 (94.6)	150 (96.8)
Indeterminate Exposure	7 (3.7)	10 (5.4)	5 (3.2)

Exposed – A patient has taken isotretinoin within 30 days of conception

Indeterminate – It is unknown if a patient has taken isotretinoin within 30 days of conception

Timing of Conception Relative to Isotretinoin Exposure

Timing of Conception	Year 3 (N=190) N (%)	Year 4 (N=186) N (%)	Year 5 (N=155) N (%)
Prior to starting isotretinoin treatment	19 (10)	16 (8.6)	9 (5.8)
During isotretinoin treatment	123 (64.7)	120 (64.5)	94 (60.6)
Within 30 days after isotretinoin treatment completion	27 (14.2)	26 (14)	13 (8.4)
Unknown ^a	21 (11.1)	24 (12.9)	39 (25.2) ^b

^a Includes indeterminate exposures

^b More indeterminate exposures occurred in Year 5 due to changes in the reporting period and a number of these are expected to be reclassified based on follow-up data in subsequent iPLEDGE reporting periods.

Most Common Reasons Determined in RCA for Pregnancy*

1. Did not use 2 forms of birth control
2. Contraceptive failure
3. Unsuccessful at abstinence

External/Non-Contraceptive Factors for Pregnancy:

- Took left-over medication

*Categories are not mutually exclusive. Patients may appear in multiple categories.

Patients Who Took Leftover Isotretinoin and Became Pregnant

- From March 1, 2006 to February 28, 2011 there were twenty-one (21) patients who took leftover isotretinoin and had an exposed pregnancy.

Pregnant Prior to Treatment (PPT) Cases with Stakeholder Non-Compliance

- From March 1, 2006 to February 28, 2011 there were nine (9) PPT cases where stakeholder non-compliance resulted in the patient receiving an isotretinoin fill while pregnant:
 - Prescriber entered a non-existent pregnancy test to confirm an FCBP (1). Note: This prescriber was deactivated.
 - Prescriber entered a non-existent pregnancy test to confirm an FCBP (1). Note: This prescriber had left the practice at which the non-compliance occurred and was not able to be located.
 - Designee entered a non-existent pregnancy test to confirm an FCBP (1). Note: This designee was deactivated.
 - Designee entered a non-existent negative pregnancy test and then called in a prescription for the FCBP without the prescriber's authorization (1). Note: This designee was deactivated.
 - Prescribers entered incorrect dates of specimen collections for FCBPs (5). The incorrect dates resulted in drug dispensed outside the 7-day window. Note: None of these actions were intentional thus the prescribers were re-educated.

Pregnant Patients Who Received Isotretinoin without a Risk Management Authorization

- From March 01, 2006 to February 28, 2011, non-compliance was confirmed for 29 iPLEDGE pregnancy cases where isotretinoin was dispensed without an RMA.
 - Dispensing isotretinoin without obtaining an RMA is the most common pharmacy deviation
 - Because of the importance of the RMA to the iPLEDGE ETASU, the sponsors are implementing the enhancement that requests prescription fill information from prescribers and patients when an RMA is not detected in the system

Unintended Pregnancy Rates in U.S.

- The rate of pregnancies reported in the general population for females in the United States who experience an unintended pregnancy is 5.1%* (51/1000).
 - Women ages 15-44
 - 48% used contraception in the month of conception
- In iPLEDGE Year 5, an unintended pregnancy rate of 0.120% (1.20/1000) was observed in FCBP Patients that had at least one isotretinoin prescription in iPLEDGE.

Note: A limitation of calculating the iPLEDGE pregnancy rate is that end of therapy and post therapy pregnancy tests are often not conducted. Therefore, the rate may be understated.

*Finer, L.B. and Henshaw, S.K. (2006). Disparities in Rates of Unintended Pregnancy in the United States, 1994 and 2001, *Perspectives on Sexual Reproductive Health*, 38(2): 90-96.

iPLEDGE Pregnancy Rate for Years 3, 4 and 5

% of Pregnancies in FCBPs with at least One Prescription Fill			
iPLEDGE Year	Year 3	Year 4	Year 5
With at least 1 RMA during Report Year	140,307	149,509	129,554
iPLEDGE Pregnancies at Time of the Year 5 Report	190	186	155
% of Pregnant Pts with at least 1 RMA during Report Year	0.1354	0.1244	0.1196



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