

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

JOINT MEETING OF THE NONPRESCRIPTION
DRUGS ADVISORY COMMITTEE (NDAC) AND THE
OBSTETRICS, REPRODUCTIVE AND UROLOGIC
DRUGS ADVISORY COMMITTEE (ORUDAC)

Virtual Meeting

Day 1

Tuesday, May 9, 2023

9:30 a.m. to 5:45 p.m.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

Meeting Roster

DESIGNATED FEDERAL OFFICER (Non-Voting)

Moon Hee V. Choi, PharmD

Division of Advisory Committee and
Consultant Management
Office of Executive Programs, CDER, FDA

NONPRESCRIPTION DRUGS ADVISORY COMMITTEE MEMBERS

(Voting)

Elma D. Baron, MD

Professor of Dermatology
Case Western Reserve University School of
Medicine
Department of Dermatology
Veterans Affairs of Northeast Ohio
Cleveland, Ohio

1 **Maria C. Coyle, PharmD, FCCP,**

2 **BCPS, BCACP, CLS**

3 *(Chairperson)*

4 Associate Clinical Professor

5 The Ohio State University College of Pharmacy

6 Columbus, Ohio

7

8 **Paul Pisarik, MD, MPH, FAAFP**

9 Geriatric Physician

10 Archwell Health

11 Tulsa, Oklahoma

12

13 **Katalin E. Roth, JD, MD**

14 Professor of Medicine

15 Division of Geriatrics and Palliative Medicine

16 Medical Faculty Associates

17 The George Washington University School of

18 Medicine and Health Sciences

19 Washington, District of Columbia

20

21

22

1 **Leslie Walker-Harding, MD, FAAP, FSAHM**

2 Ford/Morgan Endowed Professor & Chair,
3 Department of Pediatrics, Associate Dean,
4 University of Washington;
5 Chief Academic Officer & Senior Vice
6 President, Seattle Children's Hospital
7 Seattle, Washington

8
9 **NONPRESCRIPTION DRUGS ADVISORY COMMITTEE MEMBERS**

10 **(Non-Voting)**

11 **Mark E. Dato, MD, PhD**

12 *(Industry Representative)*

13 Retired: Director, Global Technology, Procter
14 and Gamble Healthcare
15 Evanston, Illinois

16
17 **OBSTETRICS, REPRODUCTIVE AND UROLOGIC DRUGS**

18 **ADVISORY COMMITTEE MEMBERS (Voting)**

19 **Margery Gass, MD**

20 Professor of Clinical Emerita
21 University of Cincinnati College of Medicine
22 Cincinnati, Ohio

1 **Pamela A. Shaw, PhD**

2 Senior Investigator

3 Biostatistics Unit

4 Kaiser Permanente Washington

5 Health Research Institute

6 Seattle, Washington

7

8 **OBSTETRICS, REPRODUCTIVE AND UROLOGIC DRUGS**

9 **ADVISORY COMMITTEE MEMBERS (Non-Voting)**

10 **Michelle C. Fox, MD, MPH, FACOG**

11 *(Industry Representative)*

12 Distinguished Investigator, Global Clinical

13 Development

14 Merck Research Laboratories

15 Rahway, New Jersey

16

17 **TEMPORARY MEMBERS (Voting)**

18 **Deborah K. Armstrong, MD**

19 Professor of Oncology

20 Professor of Gynecology and Obstetrics

21 Johns Hopkins Kimmel Cancer Center

22 Baltimore, Maryland

1 **Cynthia Baur, PhD**

2 Director, Horowitz Center for Health Literacy
3 Horowitz Endowed Chair in Health Literacy
4 University of Maryland (UMD) School of Public
5 Health
6 UMD Pandemic Preparedness Initiative Co-Director
7 Maryland Consumer Health Information Hub
8 Director
9 College Park, Maryland

10

11 **Abbey Berenson, MD, PhD**

12 Professor, Departments of Ob/Gyn and Pediatrics
13 Director
14 Center for Interdisciplinary Research in
15 Women's Health
16 University of Texas Medical Branch
17 Galveston, Texas

18

19

20

21

22

1 **Elise D. Berlan, MD, MPH, FAAP**

2 Professor of Clinical Pediatrics

3 The Ohio State University College of Medicine

4 Faculty Physician

5 Division of Adolescent Medicine

6 Nationwide Children's Hospital

7 Columbus, Ohio

8

9 **Jesse Catlin, PhD**

10 Professor of Marketing

11 College of Business

12 California State University, Sacramento

13 Sacramento, California

14

15 **Kathryn Curtis, PhD**

16 Health Scientist, Division of Reproductive

17 Health

18 Centers for Disease Control and Prevention

19 Atlanta, Georgia

20

21

22

1 **Eve Espey, MD, MPH**

2 Distinguished Professor and Chair

3 Department of Obstetrics and Gynecology

4 University of New Mexico

5 Albuquerque, New Mexico

6

7 **Sabrina Everhart**

8 *(Patient Representative)*

9 Charlestown, Indiana

10

11 **Jolie Haun, PhD, EdS**

12 Supervisory Research Health Scientist,

13 Research Service

14 James A. Haley Veterans' Hospital

15 Veterans' Health Administration

16 Tampa, Florida

17 Adjunct Associate Professor

18 Division of Epidemiology

19 Department of Internal Medicine

20 University of Utah

21 Salt Lake City, Utah

22

1 **Suzanne B. Robotti**

2 *(Consumer Representative)*

3 President

4 MedShadow Foundation

5 Executive Director

6 DES Action USA

7 New York, New York

8

9 **FDA PARTICIPANTS (Non-Voting)**

10 **Peter Stein, MD**

11 Director

12 Office of New Drugs (OND)

13 CDER, FDA

14

15 **Karen Minerve Murry, MD**

16 Deputy Director

17 Office of Nonprescription Drugs (ONPD)

18 OND, CDER, FDA

19

20

21

22

1 **Pamela Horn, MD**

2 Director

3 Division of Nonprescription Drugs II (DNPDI)

4 ONPD, OND, CDER, FDA

5

6 **Christine P. Nguyen, MD**

7 Deputy Director

8 Office of Rare Diseases, Pediatrics, Urologic

9 and Reproductive Medicine (ORPURM)

10 OND, CDER, FDA

11

12 **Audrey Gassman, MD**

13 Deputy Director

14 Division of Urology, Obstetrics, and

15 Gynecology (DUOG)

16 ORPURM, OND, CDER, FDA

17

18 **Barbara Cohen, MPA**

19 Social Science Analyst

20 DNPDI, ONPD, OND, CDER, FDA

21

22

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

Jeena Jacob, MD, PharmD

Medical Officer

DNPD II, ONPD, OND, CDER, FDA

Anandi Kotak, MD, MPH

Medical Officer

DUOG, ORPURN, OND, CDER, FDA

1	C O N T E N T S	
2	AGENDA ITEM	PAGE
3	Call to Order	
4	Maria Coyle, PharmD, FCCP, BCPS,	16
5	BCACP, CLS	
6	Introduction of Committee	
7	Moon Hee Choi, PharmD	16
8	Conflict of Interest Statement	
9	Moon Hee Choi, PharmD	24
10	FDA Opening Remarks	
11	Pamela Horn, MD	28
12	Applicant Presentations - Laboratoire HRA	
13	Pharma	
14	Introduction	
15	Helene Guillard, PharmD	32
16	Need for Nonprescription Oral Contraception	
17	Carolyn Westhoff, MD, Msc	38
18	Consumer Behavior Studies and ACCESS	
19	Study Design	
20	Self-Selection Results	
21	Russell Bradford, MD, MSPH	48
22		

1	C O N T E N T S (continued)	
2	AGENDA ITEM	PAGE
3	Clinical Interpretation of Potential Risk	
4	of POP Use in Breast Cancer Survivors	
5	Pamela Goodwin, MD, Msc, FRCPC, FASCO	70
6	ACCESS Actual Use Adherence Results	
7	Irene Laurora, PharmD	76
8	Expert Interpretation of ACCESS	
9	Adherence Results	
10	Arthur Stone, PhD	93
11	ACCESS Actual Use Adherence Conclusions	
12	Irene Laurora, PharmD	101
13	Clinical Interpretation of ACCESS	
14	Results and Considerations Around	
15	Effectiveness	
16	Stephanie Sober, MD, MSHP	104
17	Clinical Perspective	
18	Anna Glasier, MD, Dsc, OBE	114
19	Clarifying Questions	125
20		
21		
22		

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

C O N T E N T S (continued)

AGENDA ITEM	PAGE
FDA Presentations	
Introduction	
Pamela Horn, MD	150
Efficacy and Safety of Prescription	
Norgestrel Tablet and Implications for the	
Nonprescription Setting	
Anandi Kotak, MD, MPH	155
Consumer Behavior Studies (Label	
Comprehension, Targeted Breast Cancer	
Self-Selection and Self-Selection in ACCESS)	
Barbara Cohen, MPA	187
ACCESS Study Use Phase: Design and Conduct	
Jeena Jacob, MD, PharmD	218
ACCESS Study Use Phase: Use and	
Adherence Endpoints	
Rongmei Zhang, PhD	229

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

C O N T E N T S (continued)

AGENDA ITEM	PAGE
ACCESS Study Use Phase: Secondary Endpoints and Safety Findings from Uncontrolled and Postmarketing Data Jeena Jacob, MD, PharmD	238
Summary Pamela Horn, MD	249
Clarifying Questions	255
Open Public Hearing	280
Adjournment	401

P R O C E E D I N G S

(9:30 a.m.)

Call to Order

DR. COYLE: Good morning, and welcome. I would first like to remind everyone to please mute your line when you're not speaking. For media and press, the FDA press contact is Jeremy Kahn. His email is currently displayed.

My name is Maria Coyle, and I will be chairing this meeting. I will now call the May 9-10, 2023 Joint Meeting of the Nonprescription Drugs Advisory Committee and the Obstetrics, Reproductive and Urologic Drugs Advisory Committees to order. Dr. Moon Hee Choi is the designated federal officer for this meeting and will begin with introductions.

Introduction of Committee

DR. CHOI: Good morning. My name is Moon Hee Choi, and I am the designated federal officer for this meeting. When I call your name, please introduce yourself by stating your name and affiliations.

1 Dr. Baron?

2 DR. BARON: Good morning. I'm Elma Baron.
3 I'm joining you from Northeast Ohio, outside of
4 Cleveland. I am professor of dermatology at Case
5 Western Reserve University, and I am the service
6 chief of dermatology at the VA in Northeast Ohio.

7 DR. CHOI: Dr. Coyle?

8 DR. COYLE: Good morning. I'm Maria Coyle
9 from The Ohio State University College of Pharmacy,
10 where I serve as an associate professor and also
11 practitioner at our Ohio State Wexner Medical
12 Center.

13 DR. CHOI: Dr. Pisarik?

14 DR. PISARIK: I'm Dr. Paul Pisarik, family
15 physician at Archwell Health in Tulsa Oklahoma.

16 DR. CHOI: Dr. Roth?

17 DR. ROTH: Good morning. I'm a professor of
18 medicine in the Division of Geriatrics and
19 Palliative Care at George Washington University,
20 Medical Faculty Associates in Washington, DC. Good
21 morning.

22 DR. CHOI: Dr. Leslie Walker?

1 DR. WALKER-HARDING: Good morning. I'm
2 Leslie Walker-Harding. I'm chair of the Department
3 of Pediatrics at the University of Washington and
4 chief academic officer at Seattle Children's
5 Hospital, and I'm an adolescent medicine physician
6 by specialty.

7 DR. CHOI: Dr. Dato?

8 DR. DATO: Good morning. Mark Dato. I'm
9 the industry representative for the Nonprescription
10 Drug Advisory Committee, pediatric pulmonologist by
11 training.

12 DR. CHOI: Dr. Gass?

13 DR. GASS: Margery Gass, professor emeritus
14 of obstetrics and gynecology from the University of
15 Cincinnati.

16 DR. CHOI: Dr. Shaw?

17 DR. SHAW: Good morning, everyone. My name
18 is Pamela Shaw. I'm senior investigator of
19 biostatistics at the Kaiser Permanente Washington
20 Health Research Institute. Good morning.

21 DR. CHOI: Dr. Fox?

22 DR. FOX: Good morning. My name is Michelle

1 Fox. I'm an OB/GYN and representing industry
2 representative. I currently work for Merck
3 Pharmaceuticals.

4 DR. CHOI: Dr. Armstrong?

5 DR. ARMSTRONG: I'm Deb Armstrong. I'm a
6 medical oncologist at Johns Hopkins in Baltimore,
7 Maryland; professor of oncology and professor of
8 gynecology and obstetrics. I specialize in breast
9 cancer, gynecologic cancers, and cancer genetics,
10 and I'm a former member and chair of the Oncology
11 Drugs Advisory Committee.

12 DR. CHOI: Dr. Baur?

13 DR. BAUR: Good morning. I'm Dr. Cynthia
14 Baur. I am the director of the Horowitz Center for
15 Health Literacy at the University of Maryland
16 School of Public Health.

17 DR. CHOI: Dr. Berenson?

18 DR. BERENSON: Good morning. I am Abby
19 Berenson, a professor of obstetrics and gynecology
20 at the University of Texas Medical Branch, and I
21 also serve as director of the Center for
22 Interdisciplinary Research in Women's Health.

1 DR. CHOI: Dr. Berlan?

2 DR. BERLAN: Good morning. I'm Elise
3 Berlan. I am a professor of clinical pediatrics at
4 The Ohio State University College of Medicine, and
5 I'm a faculty physician in the Division of
6 Adolescent Medicine at Nationwide Children's
7 Hospital. I'm an adolescent specialist in sexual
8 and reproductive health care.

9 DR. CHOI: Dr. Catlin?

10 DR. CATLIN: Good morning, everyone. I'm
11 Jesse Catlin and professor of marketing, California
12 State University, Sacramento.

13 DR. CHOI: Dr. Curtis?

14 DR. CURTIS: Good morning, everyone. I'm
15 Kate Curtis. I'm an epidemiologist in the Division
16 of Reproductive Health at the Centers for Disease
17 Control and Prevention in Atlanta, Georgia.

18 DR. CHOI: Ms. Everhart?

19 MS. EVERHART: Good morning. My name is
20 Sabrina Everhart, and I'm the patient
21 representative out of Charlestown, Indiana..

22 DR. CHOI: Dr. Haun?

1 DR. HAUN: Good morning. My name is
2 Dr. Jolie Haun. I'm a supervisory research health
3 scientist at the James A. Haley Veterans Hospital
4 within the Veterans Health Administration in Tampa,
5 Florida, with expertise in health literacy. I'm
6 also an adjunct associate professor within the
7 Division of Epidemiology and the Department of
8 Internal Medicine at the University of Utah in Salt
9 Lake City, Utah.

10 DR. CHOI: Ms. Robotti?

11 MS. ROBOTTI: Hi. Suzanne Robotti. I'm the
12 consumer representative, and I am the founder of
13 MedShadow Foundation and the executive director of
14 DES Action USA.

15 DR. CHOI: Dr. Stein?

16 DR. STEIN: Peter Stein, director of the
17 Office of New Drugs, in the Center for Drug
18 Evaluation and Research, FDA.

19 DR. CHOI: Dr. Murry?

20 DR. MURRY: Karen Murry, deputy director,
21 Office of Nonprescription Drugs, FDA.

22 DR. CHOI: Dr. Horn?

1 DR. HORN: Good morning. Pamela Horn,
2 director, Division of Nonprescription Drugs II,
3 FDA.

4 DR. CHOI: Dr. Nguyen?

5 DR. NGUYEN: Good morning. Christine
6 Nguyen, deputy director, Office of Rare Diseases,
7 Pediatrics, Urologic, and Reproductive Products in
8 Office of New Drugs, FDA.

9 DR. CHOI: Dr. Gassman?

10 DR. GASSMAN: Audrey Gassman, deputy
11 director, Division of Urologic and Obstetrics at
12 the FDA.

13 DR. CHOI: Ms. Cohen?

14 MS. COHEN: Good morning. I'm Barbara
15 Cohen, social science analyst in the Division of
16 Nonprescription Drugs II at FDA.

17 DR. CHOI: Dr. Jacob?

18 DR. JACOB: Good morning. Jeena Jacob,
19 clinical reviewer, Division of Nonprescription
20 Drugs II.

21 DR. CHOI: Dr. Kotak?

22 DR. KOTAK: Good morning. Anandi Kotak,

1 medical officer, Division of Urology, Obstetrics,
2 and Gynecology, FDA.

3 DR. CHOI: Thank you.

4 DR. COYLE: For topics such as those being
5 discussed at this meeting, there are often a
6 variety of opinions, some of which are quite
7 strongly held. Our goal is that this meeting will
8 be a fair and open forum for discussion of these
9 issues and that individuals can express their views
10 without interruption. Thus, as a gentle reminder,
11 individuals will be allowed to speak into the
12 record only if recognized by the chairperson. We
13 look forward to a productive meeting.

14 In the spirit of the Federal Advisory
15 Committee Act and the Government in the Sunshine
16 Act, we ask that the advisory committee members
17 take care that their conversations about the topic
18 at hand take place in the open forum of the
19 meeting.

20 We are aware that members of the media are
21 anxious to speak with the FDA about these
22 proceedings; however, FDA will refrain from

1 discussing the details of this meeting with the
2 media until its conclusion. Also, the committee is
3 reminded to please refrain from discussing the
4 meeting topic during breaks or lunch. Thank you.

5 Dr. Moon Hee Choi will read the Conflict of
6 Interest Statement for the meeting.

7 **Conflict of Interest Statement**

8 DR. CHOI: The Food and Drug Administration
9 is convening today's Joint Meeting of the
10 Nonprescription Drugs Advisory Committee and the
11 Obstetrics, Reproductive and Urologic Drugs
12 Advisory Committee. With the exception of the
13 industry representatives, all members and temporary
14 voting members of the committees are special
15 government employees or regular federal employees
16 from other agencies, and are subject to federal
17 conflict of interest laws and regulations.

18 The following information on the status of
19 this committee's compliance with federal ethics and
20 conflict of interest laws, covered by but not
21 limited to those found at 18 U.S.C. Section 208, is
22 being provided to participants in today's meeting

1 and to the public.

2 FDA has determined that members and
3 temporary voting members of these committees are in
4 compliance with federal ethics and conflict of
5 interest laws. Under 18 U.S.C. Section 208,
6 Congress has authorized FDA to grant waivers to
7 special government employees and regular federal
8 employees who have potential financial conflicts
9 when it is determined that that agency's need for a
10 special government employee's services outweighs
11 his or her potential financial conflict of
12 interest, or when the interest of a regular federal
13 employee is not so substantial as to be deemed
14 likely to affect the integrity of the services
15 which the government may expect from the employee.

16 Related to the discussions of today's
17 meeting, members and temporary voting members of
18 these committees have been screened for potential
19 financial conflicts of interests of their own as
20 well as those imputed to them, including those of
21 their spouses or minor children and, for purposes
22 of 18 U.S.C. Section 208, their employers. These

1 interests may include investments; consulting;
2 expert witness testimony; contracts, grants,
3 CRADAs; teaching, speaking, writing; patents and
4 royalties; and primary employment.

5 Today's agenda involves the discussion of
6 supplemental new drug application, sNDA,
7 017031/S-041, for Opill, norgestrel, Tablet,
8 0.075 milligram, submitted by Laboratoire HRA
9 Pharma. Opill is proposed for nonprescription use
10 as a once daily oral contraceptive to prevent
11 pregnancy. This is a particular matters meeting
12 during which specific matters related to
13 Laboratoire HRA Pharma's sNDA will be discussed.

14 Based on the agenda for today's meeting and
15 all financial interests reported by the committee
16 members and temporary voting members, no conflict
17 of interest waivers have been issued in connection
18 with this meeting. To ensure transparency, we
19 encourage all standing committee members and
20 temporary voting members to disclose any public
21 statements that they have made concerning the
22 product at issue.

1 With respect to FDA's invited industry
2 representatives, we would like to disclose that
3 Dr. Mark Dato and Dr. Michelle Fox are
4 participating in this meeting as non-voting
5 industry representatives, acting on behalf of a
6 regulated industry. Dr. Dato's and Dr. Fox's role
7 at this meeting is to represent industry in general
8 and not any company. Dr. Dato is retired and
9 Dr. Fox is employed by Merck Research Laboratories.

10 We would like to remind members and
11 temporary voting members that if the discussions
12 involve any other products or firms not already on
13 the agenda for which an FDA participant has a
14 personal or imputed financial interest, the
15 participants need to exclude themselves from such
16 involvement, and their exclusion will be noted for
17 the record. FDA encourages all other participants
18 to advise the committees of any financial
19 relationships that they may have with the firm at
20 issue. Thank you.

21 DR. COYLE: We will now proceed with FDA
22 introductory remarks from Dr. Pamela Horn.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

FDA Opening Remarks - Pamela Horn

DR. HORN: Good morning, and welcome to the Joint Meeting of the Nonprescription and Obstetrics, Reproductive and Urologic Drugs Advisory Committees. My name is Pamela Horn. I'm the director of Division of Nonprescription Drugs II in the Office of New Drugs.

Thank you for joining us for this important discussion of an application to switch norgestrel tablet from the prescription to nonprescription setting today. I would especially like to thank the advisory committee members who have taken the time out of their very busy schedules to help us consider this application, as well as the many members of professional groups and the public who will be testifying and have written comments to the docket.

FDA appreciates the importance of promoting reproductive health in the U.S. We acknowledge the complexities of this, particularly as it pertains to family planning, which includes emergency contraception for which there are currently two

1 approved drugs, one of which is available without a
2 prescription, and various contraceptive methods,
3 including birth control pills. Today, we will not
4 discuss all these topics, rather we will focus the
5 discussion on one type of birth control pill,
6 norgestrel tablet, which has one hormone, and not
7 the combined birth control pill, which has two
8 hormones, and consideration for whether norgestrel
9 tablet would be safe and effective without a
10 prescription.

11 As a person who has devoted my career thus
12 far to public health, and a person who cares deeply
13 about women's health, I'm driven to make
14 recommendations and decisions that will improve
15 women's health. I would love to have unambiguous
16 data to support these recommendations and
17 decisions, but my years of experience in regulatory
18 science have taught me that this is rarely the
19 case, and today is no exception.

20 We have an application to discuss with many
21 complicated issues and uncertainties, including
22 data with questionable reliability. FDA and this

1 review team are committed to making the best
2 decision that we can with the information available
3 to us. We are acutely aware of the importance of
4 this application, and we have worked extremely hard
5 to bring you the most comprehensive and thoughtful
6 evaluation of it that we can.

7 This morning, we will be hearing
8 presentations from the applicant, and this
9 afternoon, we will be hearing presentations from
10 FDA. After that, we will be hearing from the
11 public presenters. We thank the persons presenting
12 verbally, as well as the many of you for writing to
13 the public docket. Your perspectives are important
14 to our decision making.

15 Tomorrow will be devoted to discussion and a
16 vote by the committee members. Our goal is to
17 obtain comprehensive input to make a sound
18 scientific regulatory decision that will have the
19 best possible outcome for public health in the U.S.
20 We look forward to a thorough and thoughtful
21 discussion of this application. Thank you.

22 DR. COYLE: Thank you.

1 Both the Food and Drug Administration, FDA,
2 and the public believe in a transparent process for
3 information gathering and decision making. To
4 ensure such transparency at the advisory committee
5 meeting, FDA believes that it is important to
6 understand the context of an individual's
7 presentation.

8 For this reason, FDA encourages all
9 participants, including the applicant's
10 non-employee presenters, to advise the committee of
11 any financial relationships that they may have with
12 the applicant, such as consulting fees, travel
13 expenses, honoraria, and interest in the applicant,
14 including equity interests and those based on the
15 outcome of the meeting.

16 Likewise, FDA encourages you at the
17 beginning of your presentation to advise the
18 committee if you do not have any such financial
19 relationships. If you choose not to address this
20 issue of financial relationships at the beginning
21 of your presentation, it will not preclude you from
22 speaking.

1 We will now proceed with the Laboratoire HRA
2 Pharma's presentation.

3 **Applicant Presentation - Helene Guillard**

4 DR. GUILLARD: Good morning. I'm Helene
5 Guillard, global Rx-OTC switch director, Women's
6 Health, at HRA Pharma, a Perrigo company. I'd like
7 to thank the chair, members of the committee, and
8 FDA for the opportunity to discuss the switch of
9 Opill for over-the-counter use. This is an
10 important day for science, public health, and
11 importantly, individual women, their partners,
12 families, and communities. With this in mind, I
13 also want to thank the many thousands of people who
14 participated in our clinical program.

15 On May 1960, a pill for oral contraception
16 was approved in the U.S. for the very first time,
17 and exactly 63 years to the day, we are in this
18 meeting to discuss making an old contraceptive pill
19 available over the counter for the first time in
20 history. Today, you will give careful
21 consideration to this important clinical
22 application, and no doubt, the results of your

1 deliberations will have far-reaching impact.

2 Even women who want children at some point
3 in their lives spend most of their reproductive
4 years trying to avoid pregnancy; however, women in
5 the U.S. face unnecessary burdens in accessing
6 effective contraception and, unfortunately, the
7 nonprescription options are limited to the least
8 effective methods, such as condoms or withdrawal.
9 Opill is a more effective option than all current
10 nonprescription methods.

11 Today, we'll show you data demonstrating
12 that using the proposed OTC labeling, women of all
13 reproductive ages can use Opill safely and
14 effectively without healthcare provider
15 supervision. Opill has the key characteristics of
16 an OTC drug. Importantly, improved access to Opill
17 has the potential to reduce unintended pregnancy in
18 the U.S.

19 Let me provide some brief background on
20 Opill. Opill is a prescription daily
21 progestin-only contraceptive pill or POP. The
22 active ingredient is norgestrel and the daily dose

1 is 0.075 micrograms. Each pack includes blisters
2 of 28 tablets and users simply need to take one
3 pill every day with no break between packs. This
4 product isn't new. It's been marketed for more
5 than 30 years. During that time, 17 million packs
6 have been sold in the U.S.

7 POPs have well-characterized clinical
8 efficacy and safety profiles, and they're
9 considered safe. POPs prevent conception by
10 thickening the cervical mucus to inhibit sperm
11 penetration, as well as suppressing or disrupting
12 ovulation.

13 So now, the questions about the benefit-risk
14 assessment of making Opill available OTC; Opill is
15 a safe and effective contraceptive already approved
16 by FDA. The inherent efficacy and safety of Opill
17 is the same whether it's prescribed by a physician
18 or purchased over the counter. Thus, let's discuss
19 the impact of consumers using Opill as guided by
20 the OTC labeling.

21 On the benefit side, which is what's called
22 the incremental benefits, it's, for instance, the

1 improved access to an effective contraceptive, as
2 well as what that means, such as reducing
3 unintended pregnancy and its consequences. On the
4 risk side, which was called the incremental risk,
5 it's, for instance, how likely is it that the user
6 wrongly selects the product or uses it incorrectly,
7 and if so, what could be the clinical impact.

8 So ultimately, here is the crucial question.
9 Can consumers, supported by the label, select and
10 use Opill safely and effectively in the OTC setting
11 so that the potential incremental benefits of
12 consumers using Opill, as guided by the OTC
13 labeling, outweigh the potential incremental risks?
14 Today, we'll answer that question.

15 In support of our goal to make Opill
16 available OTC, we initiated an extensive iterative
17 label development process, which began with
18 adapting the Opill prescription labeling into
19 consumer-friendly language. The OTC Opill label is
20 informed by relevant medical guidance and follows
21 the standard format for all OTC products.

22 We tested the language on the label with

1 consumers. We revised the label many times,
2 including with feedback from the FDA. Overall, the
3 proposed OTC label was tested over a seven-year
4 development program, which comprised a total of
5 14 consumer studies involving many thousands of
6 people.

7 The proposed OTC label includes the Drug
8 Facts Label or DFL. The DFL incorporates all of
9 the information from the prescription label that
10 consumers need to properly select and use Opill in
11 the OTC setting. Our label also includes a
12 consumer information leaflet and a reminder card to
13 further support consumers in adhering to key label
14 directions.

15 Let me briefly highlight the key elements of
16 the DFL, which will be the main focus of our
17 presentation today. The Drug Facts Label has a
18 highly standardized and tightly regulated format
19 that must appear on all OTC drugs. Each contains a
20 section on use for what the product is used for, a
21 section headed, "Sexually Transmitted Disease
22 Alert" that appears on contraceptives; when not to

1 use, where consumers find the contraindications for
2 use; when to ask a doctor before use; a section
3 headed, "When using this product," telling what to
4 expect; when to seek medical attention during use;
5 a section defining when to stop use and ask a
6 doctor; and finally directions for use. With the
7 DFL, consumers should have all the information to
8 use an OTC product safely and effectively without
9 supervision of a healthcare provider.

10 Now, let me present key aspects of our
11 clinical development program for testing the OTC
12 labeling and other studies done to ensure Opill is
13 appropriate for the OTC setting. We conducted
14 several consumer studies to test how consumers
15 understand the OTC level and verify if they could
16 correctly identify if Opill is right for them, and
17 if they could use it correctly, based on the label,
18 particularly how well they would follow the dosing
19 instructions.

20 In addition, we conducted a pharmacodynamic
21 study, which we called the Delayed Pill Intake
22 Study, to assess the potential impact of missing a

1 pill or taking it late. This new data helps us
2 understand the clinical significance of failure to
3 respect the strict dosing schedule imposed by the
4 label. Lastly, we designed a model to estimate the
5 number of unintended pregnancies that use of Opill
6 OTC could prevent. We reviewed much data from our
7 program, with a particular focus in today's
8 presentation on self-selection and actual use.

9 Here is our agenda for the rest of the
10 presentation. We also have additional experts with
11 us today. All outside experts, with the exception
12 of Drs. Wilkinson and Edelman, have been
13 compensated for their time and travel to today's
14 meeting.

15 Thank you, and now turn the lectern over to
16 Dr. Westhoff.

17 **Applicant Presentation - Carolyn Westhoff**

18 DR. WESTHOFF: Hello. Good morning. I'm
19 Carolyn Westhoff. I'm professor of OB-GYN and
20 epidemiology at Columbia University, and I also
21 serve as the editor-in-chief of the journal,
22 Contraception. I'm very pleased to be here today

1 to discuss the need for OTC access to oral
2 contraception, so let me start with where we are
3 now.

4 Of the roughly 6 million pregnancies that
5 occur in the U.S. every year, 45 percent are
6 unintended. So despite availability of a variety
7 of contraceptive methods, nearly half of the
8 pregnancies are unintended every year. Among
9 pregnancies in adolescents aged 15 to 17, an
10 alarming 72 percent are unintended, and these
11 unintended pregnancies occur in women of all ages,
12 races, ethnicities, and socioeconomic backgrounds.

13 In the U.S., half of all women will have had
14 an unintended pregnancy by age 45, and these have
15 significant consequences. In addition to all the
16 inherent maternal health risks associated with
17 pregnancy, an unintended pregnancy also includes
18 increased risk of pregnancy loss and delayed
19 prenatal care. These women also have a 2-fold
20 higher rate of postpartum depression compared to
21 women whose pregnancy was planned. For the child,
22 risks include prematurity, low birth weight, and

1 greater infant mortality.

2 In addition, there's an increased risk of
3 lower educational and economic attainment for the
4 woman herself and her children. In fact, only
5 about 50 percent of teen mothers receive a high
6 school diploma by age 22. Effective contraception
7 is the best way to reduce unintended pregnancy and
8 its negative consequences.

9 The U.S. government has identified
10 preventing unintended pregnancies as a public
11 health priority. This goal specifically includes
12 decreasing pregnancies in adolescents, as well as
13 increasing the proportion of women and adolescent
14 females who use effective birth control. This
15 chart shows the contraceptive methods available in
16 the U.S. and the typical failure rates associated
17 with each; and the reason we use typical use
18 failure rates is because they reflect use in the
19 real world, not in clinical trials.

20 In the top row are the most effective
21 methods, from permanent ones such as sterilization,
22 to long-acting ones such as an intrauterine device.

1 In these, the typical failure rate is less than
2 1 percent. Right below are the moderately
3 effective hormonal methods such as Opill. The
4 typical failure rate for these are between
5 4 and 7 percent, which are higher than those in
6 product labels because adherence is less than
7 perfect. In the gray box in the middle are the
8 less effective methods such as condoms. They have
9 a typical failure rate of 13 to 27 percent.
10 Finally, using no birth control at all carries a
11 greater than 85 percent chance of pregnancy over
12 one year.

13 The red line divides methods available with
14 and without a prescription. Those shown above the
15 red line, the moderately to most effective methods,
16 are all only available by prescription. Shown
17 below the red line are the less effective methods,
18 those with higher failure rates. These are not
19 simply less effective; they also require correct
20 action at the time of every active intercourse, and
21 they may require experience or training for
22 effective use.

1 In addition, male condoms, withdrawal, and
2 fertility awareness based methods require the
3 active involvement of the woman's partner, and in
4 most cases do not allow for discreet use by the
5 woman. What this means to me is that we need more
6 effective methods to be available without a
7 prescription; then people can more easily prevent
8 unintended pregnancy by moving from less effective
9 methods, below the red line, to the more effective
10 methods.

11 How does this all relate to current use?
12 There are about 72 million women of reproductive
13 age in the U.S., and 40 million are at risk for an
14 unintended pregnancy. Approximately 15 million of
15 these 40 million women, outlined in red on the
16 right, use the less effective methods or no method
17 at all. Most women will use a variety of methods
18 over their reproductive lives, but what's important
19 is that individual women who want to avoid
20 pregnancy should have uncomplicated access to an
21 effective contraceptive that works for them and
22 their lifestyle.

1 Unfortunately, women currently face barriers
2 to initiating and refilling the more effective
3 methods since they are only available by
4 prescription. These barriers include not having a
5 medical provider or insurance, difficulty
6 scheduling an appointment, and the time and cost of
7 getting there.

8 These barriers are real. A range of studies
9 show approximately a third of women whoever tried
10 to obtain a prescription or refill for a pill,
11 patch, or ring reported difficulties. Between
12 40 and 50 percent said they didn't use
13 contraception because they ran out and weren't able
14 to get more, and about a third said they simply
15 couldn't get their next supply in time. A woman
16 who wants to avoid pregnancy needs better access to
17 effective contraceptives, and this includes all
18 women, including adolescents.

19 While very few young adolescent females have
20 ever had sex, by the age of 17, about 50 percent
21 are sexually active, and these youngest women face
22 the most significant barriers to accessing the more

1 effective methods. Here's what we know. In 2017,
2 the most recent year when pregnancy data are
3 available, there were 88,000 pregnancies in
4 adolescents 17 and younger, and in 2021, there were
5 37,000 births in adolescents 17 and younger.

6 A recent CDC publication reported 30 percent
7 of first births in the U.S. occurred during the
8 teenage years. CDC recommendations on safe use of
9 contraceptive methods imposes no age restriction on
10 oral contraceptive use. In addition, many medical
11 organizations strongly endorse adolescent access to
12 OTC oral contraceptives. In fact, leading medical
13 societies representing a broad range of physicians,
14 including the American College of OB-GYN, the AMA,
15 the American Academy of Family Physicians, and
16 experts in adolescent health, all support
17 availability of over-the-counter oral
18 contraception, as do the vast majority of women in
19 the U.S.

20 Let me tell you a bit about the reality of
21 contraceptive prescribing. First, oral
22 contraception is easy to use, safe, and generally

1 appropriate for most women. Women do not need to
2 see a healthcare provider to go on an oral
3 contraceptive. The reality is that when we
4 prescribe an oral contraceptive, we typically won't
5 see our patient again for a year or longer. When
6 we see a patient, we usually don't provide the
7 level of counseling that is provided in the Drug
8 Facts Label, nor do we oversee product use or
9 adherence, nor can we repeatedly emphasize to a
10 patient about using the pills every day at the same
11 time.

12 Let me briefly discuss this last point.
13 Data tell us that adherence to all types of daily
14 prescription medications is less than perfect.
15 This is especially true for preventive medications,
16 including oral contraceptives. Multiple studies
17 show that approximately 15 percent of women miss
18 three or more active pills per cycle in the
19 prescription setting. That translates to missing
20 3 out of 21 active pills, or 15 percent, of the
21 pack. We also know from national data that about
22 7 percent of women report an unintended pregnancy

1 during their first year of typical prescription OC
2 use. These real-world data provide reference
3 points for considering the sponsor's data on OTC
4 use.

5 Before I conclude, I want to take a moment
6 to address a few important differences in the two
7 types of oral contraceptives we have today. POPs
8 and combined OCs have the same typical use
9 effectiveness, but there are some differences. Due
10 to its different mechanism of action, women can
11 experience more irregular bleeding, such as
12 spotting or no bleeding at all when using a POP
13 rather than a COC. Importantly, this type of
14 bleeding is not medically concerning.

15 While both POPs and COCs have the same
16 typical use effectiveness, POPs are recommended to
17 be taken at the same time each day within 3 hours;
18 whereas the recommendation for COCS is simply to
19 take the pills at the same time each day. The
20 sponsor will show new data later, suggesting that
21 neither missing a pill nor taking one late appear
22 to jeopardize potential contraceptive efficacy of

1 the POP.

2 The biggest difference between POPs and COCs
3 is that POPs, such as Opill, do not contain
4 estrogen, and COCs do. Thus, POPs don't have the
5 increased risk of venous thromboembolism that COCs
6 have. This is also the reason CDC's medical
7 eligibility criteria list 16 conditions for
8 unacceptable health risks for COCs and only one,
9 breast cancer, for POPs. Overall, POPs carry very
10 few contraindications, making them appropriate for
11 a broad population of women.

12 The CDC medical eligibility criteria
13 classifies acceptability for contraceptive use
14 based on certain medical conditions. This slide
15 shows in red the 16 Category 4 conditions, which
16 indicate an unacceptable health risk. On the left
17 are POPs and on the right, COCs. Only breast
18 cancer is a Category 4 condition for the POP.
19 These CDC criteria are what U.S. clinicians use
20 when prescribing contraception.

21 To close, there is a need for an OTC oral
22 contraceptive in the U.S. Even with all available

1 options, almost half of U.S. pregnancies are
2 unintended. This percentage is much higher for
3 adolescents. These unintended pregnancies have
4 significant consequences for the women and their
5 families.

6 In 2023, as endorsed by the full medical
7 community, women should have ready access to oral
8 contraception. Not only is this important for the
9 woman and her family, but OTC availability of an
10 effective oral contraceptive, has the potential to
11 result in substantially improved individual
12 clinical and public health outcomes. Based on
13 their long history of safe and effective use, POPs
14 make an ideal candidate for OTC use.

15 Thank you, and I will now turn the
16 presentation over to Dr. Bradford.

17 **Applicant Presentation - Russell Bradford**

18 DR. BRADFORD: Thank you, Dr. Westhoff, and
19 good morning. I'm Russell Bradford, a practicing
20 board-certified internist and pediatrician. I'm
21 also senior vice president at PEGUS Research, a
22 contract research organization specializing in

1 consumer behavior studies, done in support of
2 prescription-to-OTC switch applications. We've
3 been in business for more than 30 years, supporting
4 many Rx-to-OTC switch programs over that time, and
5 I directly oversaw all of the associated consumer
6 behavior studies for Opill.

7 I'll briefly introduce the studies that are
8 often done to support an application to switch a
9 product from prescription to over-the-counter
10 status. Products that are candidates for a switch
11 are already approved for prescription use, and
12 their efficacy and safety are already established.
13 Therefore, the research questions and associated
14 designs of consumer behavior studies for switch
15 programs are driven by the fact that in the OTC
16 setting, consumers are guided by product labeling,
17 principally the Drug Facts Label, without
18 supervision of a healthcare provider.

19 In an Rx-to-OTC switch program, the first
20 question is whether consumers understand the
21 messages in the proposed OTC labeling. To evaluate
22 this question, we perform label comprehension

1 studies, often refining labeled messaging in
2 response to insights from consumers and with
3 feedback from FDA. When labeling has been
4 optimized, the next question is whether the DFL
5 appropriately guides consumers as they decide if a
6 product is right for them. We answer this question
7 with self-selection studies, and for these studies,
8 we recruit participants who are potentially
9 interested in the product.

10 When there are rare but important
11 contraindications, we often conduct targeted
12 self-selection studies to test whether consumers
13 with those specific contraindications can identify
14 that the product is not appropriate for them.
15 Finally, we ask whether consumers can actually use
16 a product correctly when guided by the OTC labeling
17 by conducting what's called an actual use trial.

18 Randomized-controlled trials are designed to
19 demonstrate the effect of a drug, and therefore
20 investigators take great pains to control variables
21 like participant behavior. In contrast, AUTs are
22 much less controlled because the goal is to

1 evaluate participant behavior rather than the
2 medicine itself. In an AUT, we attempt to
3 replicate the OTC environment, and that is the
4 primary factor that influences study design. In
5 some cases, we make compromises based on those
6 design principles, which lead to a reduction in
7 control and in the level of detail that we can
8 gather from participants about their experiences.

9 Because consumer behavior studies are
10 generally observational, success in these studies
11 is not judged by strict statistical testing.
12 Instead, we establish, a priori, target performance
13 thresholds by a thoughtful appraisal of the
14 clinical consequences should consumers not follow
15 the label instructions. As FDA has noted, these
16 thresholds are targets and not automatic hard
17 stops. If an objective fails to meet a threshold,
18 the clinical impact is considered within the total
19 risk-benefit assessment.

20 We conducted several label comprehension
21 studies during the development of the Opill
22 labeling, and we found that the messages in the OTC

1 labeling are generally well understood. However,
2 because the ultimate test of label comprehension is
3 how actual users translate the OTC labeling into
4 behavior, we'll focus today on the results from the
5 pivotal self-selection and actual use trial known
6 as ACCESS.

7 ACCESS is a first-of-its-kind study because
8 while every AUT is unique, the ACCESS study
9 involved an added level of complexity in that Opill
10 is a product that is intended for continuous daily
11 preventive use rather than intermittent use for
12 symptom relief, which describes most other OTC
13 candidates.

14 In ACCESS, consumers could purchase and use
15 Opill for up to 6 months in an OTC-like setting,
16 and unlike the real world, we needed to observe and
17 measure behavior, including daily use of Opill
18 without prompting it. This is important because we
19 needed to demonstrate that consumers would behave
20 in such a way as to benefit from the
21 product -- that is, prevent unintended
22 pregnancy -- without unacceptable incremental risk;

1 that is, an increase in the risk beyond what they
2 would incur if they took the product under the
3 supervision of a healthcare provider.

4 ACCESS evaluated the adequacy of the
5 proposed OTC labeling to drive appropriate
6 self-selection and appropriate use. The ACCESS
7 study comprised four distinct phases, as I've shown
8 here, and I'll walk through each of these phases in
9 detail, focusing on the application of AUT design
10 principles to access specifically.

11 There were 36 research sites distributed
12 across the U.S. Sites were primarily community
13 pharmacies open to participants of all ages.
14 Because we anticipated that those younger than 18
15 would have greater barriers to participation, and
16 therefore would be difficult to recruit, we
17 included 10 clinic sites where patients younger
18 than 18 who were seeking oral contraceptives could
19 be invited to participate. Digital and print
20 advertisements were aimed at those interested in an
21 OTC oral contraceptive, and nearly 1900
22 participants started the screening phase.

1 In the self-selection phase of the study,
2 participants reviewed the OTC labeling and made a
3 decision about whether Opill was okay for them to
4 use. This phase of the study included anyone with
5 an interest in the product, including those who
6 were ultimately not appropriate to take the
7 product. And while this wasn't a formalized
8 process in order to mimic the OTC environment,
9 participants were free to consult a healthcare
10 professional at any time.

11 Following the selection decision,
12 participants answered a scripted series of specific
13 health-related questions so that we could determine
14 whether the product was indeed appropriate for them
15 to use. We conducted a standardized health
16 literacy assessment known as the REALM or
17 REALM-Teen. After informed consent, the remaining
18 steps, including an enrollment pregnancy test, were
19 completed. Just under 1800 participants made up
20 the self-selection population.

21 In order to proceed to the use phase,
22 participants had to purchase Opill with their own

1 money. The number of packs at initial purchase was
2 left up to them, much like an OTC experience.
3 Participants were formally trained on the use of an
4 electronic diary. The e-diary asked them to report
5 each day whether they have taken Opill on the
6 previous day and at what time; whether they had had
7 sex; and whether they used any other contraceptive
8 method. Participants then used the product in an
9 entirely self-driven manner guided only by product
10 labeling.

11 In order to avoid inadvertently impacting
12 adherence, there was no daily prompts to complete
13 the diary. Instead, each participant received a
14 standard reminder every 4 days. The e-diary was
15 deliberately designed to capture a wide range of
16 pill-taking behaviors, including taking multiple
17 doses per day, stopping and starting, and so on.

18 We also conducted periodic telephone
19 interviews with participants in which nurse
20 interviewers inquired about the use of Opill
21 generally and collected reports of adverse events.
22 These interim interviews intentionally avoided

1 asking direct questions about behaviors of interest
2 so that subsequent participant behavior would
3 remain unbiased. During the use phase,
4 participants were able to return to the study site
5 for resupply at any time; however, they could only
6 resupply at the study site where they enrolled, so
7 widespread access to the product, which is one of
8 the primary potential benefits of OTC availability,
9 could not be simulated.

10 Participants were reimbursed for all
11 purchases at the end of the study, but they were
12 not informed of that until the study was complete.
13 There were 883 participants who reported use of a
14 product in the e-diary, and they comprised the user
15 population.

16 Finally, it was only at the end of study
17 that a nurse interviewer asked specific questions
18 about selection decisions and other behaviors of
19 interest. This included whether a participant
20 interacted with a healthcare provider regarding any
21 relative contraindications or if they experienced
22 any of the conditions where the label advises to

1 talk to a healthcare provider or to stop use, and
2 whether they did. Participants were asked to
3 return any product, and an end-of-study pregnancy
4 test was administered with results available for
5 73 percent of participants.

6 Now, let me turn to the self-selection
7 results for ACCESS. The self-selection phase
8 enrolled nearly 1800 participants, and as you can
9 see, participants were racially and ethnically
10 diverse. Subpopulations of interest, namely
11 adolescents and participants with low health
12 literacy, were well represented with sample sizes
13 adequate to evaluate performance in those groups.

14 Self-selection studies assess how the Drug
15 Facts Label influences consumers' decisions about
16 using a product, so in order to do that, we
17 classify each participant on two variables: first,
18 whether they select to use the product, and second,
19 whether they are appropriate to use the product.

20 In order to classify participants on the
21 first variable, selection, we ask a series of
22 selection questions as shown here. The first

1 question relates to whether the consumer, based on
2 the label, believes the product is okay or not okay
3 for them, and why or why not. Next, we ask if they
4 would like to purchase Opill, and again, why or why
5 not.

6 Both of these questions are important to
7 understanding a consumer's thinking because not
8 infrequently, participants interpret the
9 self-selection question as asking about the
10 product's general appeal rather than whether they
11 themselves qualify to use it.

12 Here are some examples. These participants,
13 a 62-year-old female with a history of colon
14 cancer, a 25-year-old male, and a 12-year-old
15 premenarchal female, all answered yes to the
16 self-selection question, but their responses make
17 it clear that they said yes because the product
18 generally appealed to them. But importantly, each
19 of these participants said they would not purchase
20 the product, despite having said yes to the initial
21 self-selection question, because it was not
22 relevant to them. The first said she would not

1 purchase because she was menopausal, the second
2 because he was a man, and the third because she
3 didn't need it.

4 FDA's approach to selection classification
5 focuses on the basic response to the selection
6 question, so they classified each of these
7 participants and other similar participants as
8 selectors, while we classify them as non-selectors
9 based on the entirety of their response as
10 prespecified in the study protocol. Furthermore,
11 participants like this are at no risk because they
12 do not intend to use Opill. I'll be discussing the
13 implications of this difference in selector
14 classification in a few moments.

15 After the participants have made a selection
16 decision, we ask them a series of scripted
17 questions to learn whether any of the Drug Facts
18 Label messages of interest apply to them, and based
19 on those responses, we classify them as appropriate
20 to use or not.

21 For participants who select to use the
22 product, but who were classified as not appropriate

1 to use, we conducted a prespecified physician
2 review process in order to evaluate the potential
3 clinical consequences of their selection decision.
4 Three independent OB/GYNs reviewed each of these
5 participants' case books and made an assessment
6 whether it was clinically acceptable for them to
7 use Opill; that is, they would have prescribed
8 Opill had that individual chosen to use it. This
9 is important, as it ultimately helps to assess
10 whether there would be a clinical impact from these
11 participants' selection decision.

12 The messages from the Opill DFL tested in
13 ACCESS, which contribute to a participant's
14 classification as appropriate or not appropriate to
15 use, include those which aid the consumer to select
16 this product for its appropriate indication;
17 include an allergy warning; identify do-not-use
18 conditions; and finally, guide users to talk to a
19 doctor for assessment of pre-existing medical
20 conditions.

21 The cross-tabulation of selection and
22 appropriateness to use lets us populate the

1 self-selection analysis table, as shown here.
2 Group A are those who selected the product and were
3 appropriate to use. Group B are those who selected
4 to use the product but who were inappropriate to
5 use, and is the group we are most interested in, as
6 it represents those consumers for whom the
7 benefit-risk ratio might not be favorable. Group C
8 are those who did not select but who would be
9 appropriate to use.

10 Participants are asked to make an actual
11 decision based on their own situation, which often
12 encompasses factors outside of labeling; therefore,
13 participants in Group C made a decision which is
14 not incorrect and which is not associated with any
15 risk. Group D are those who are not appropriate to
16 use and who did not select the product. Therefore,
17 groups which represent correct selection decisions
18 are Group A and Group D.

19 When the self-selection table is populated,
20 we can then calculate selection measures. The
21 primary self-selection endpoint in ACCESS was the
22 proportion of participants who made a correct

1 decision from among all who made either a correct
2 or an incorrect decision. We exclude Group C
3 because while this group may be appropriate to use,
4 a decision not to select is not incorrect and is
5 associated with no risk.

6 The secondary self-selection endpoint
7 evaluates the proportion of those who were not
8 appropriate to use who made the correct decision to
9 not select the product. Both of these calculations
10 are useful in helping us understand the
11 implications of OTC availability of Opill, and when
12 we populate the self-selection table based on these
13 prespecified approaches for classifying
14 participants on the selection and appropriateness
15 to use variables, here are the numbers. These
16 12 participants are those who we classified as not
17 appropriate to use but who selected to use, and
18 therefore represent those for whom the clinical
19 benefit-risk may not be favorable.

20 Let's now look at how FDA has classified
21 those same participants in the table below. There
22 are two underlying differences between the two

1 tables. First, FDA manually reviewed a group of
2 participants evaluating each for selection and
3 appropriateness to use. This review reclassified
4 14 participants that we classified as appropriate
5 or acceptable to use, to not appropriate to use.
6 This is the difference between the 78 categorized
7 as not appropriate versus FDA's 92.

8 The larger difference between these two
9 tables is a result of FDA classifying some of the
10 participants as selectors who we considered to be
11 non-selectors. This is because FDA only considered
12 the basic okay or not okay response to the
13 self-selection question when classifying
14 participants, except for those with specific
15 conditions that they chose to review manually. In
16 contrast, our classification strategy involved a
17 systematic review of all of the information from
18 both the self-selection question and the purchase
19 question, which represents a more informative
20 reflection of a participant's actual selection
21 decision, and we did this for all participants.
22 With the understanding of these differences, let's

1 focus on Group B because this is the group of
2 clinical interest.

3 This table shows you the 67 participants
4 that fall into Group B based on the FDA analysis.
5 Fifty-five of these participants were not
6 classified by the sponsor in the same way, so I'd
7 like to take some time and walk through the
8 differences.

9 In the left-hand column are the
10 12 participants which both we and the FDA
11 classified into Group B, and to the right are the
12 55 additional participants that FDA assigned. As a
13 reminder, these additional 55 are added through a
14 combination of reclassifying some from appropriate
15 to not appropriate to use, and some from
16 non-selectors to selectors.

17 You'll recall the examples I cited earlier
18 of three participants who FDA classified as
19 selectors despite their clear indication that they
20 would not use themselves. They are included among
21 FDA's additional 55 participants; one because of a
22 history of colon cancer; one who is male; and one

1 who was premenarchal and unable to become pregnant.
2 They're included among these participants because
3 of FDA's selection classification approach.

4 I'd like to review a few additional
5 participants in detail to further illustrate why we
6 feel that our classification better reflects the
7 clinical implications of the selection decision.
8 For example, two participants reported a history of
9 breast cancer, one of whom selected to use and one
10 who indicated that she would consult a healthcare
11 provider. FDA classified her as a selector even
12 though she indicated that she would talk to a
13 healthcare provider.

14 There were 8 participants who reported
15 cancers other than breast cancer. FDA classified
16 all eight of these as not appropriate to use. The
17 OB/GYN panel classified seven of them as acceptable
18 to use because none had cancers that were
19 potentially hormone responsive. The eighth
20 remained classified as not appropriate to use
21 because she reported, what she called in her words,
22 a venereal cancer which she didn't characterize

1 further, so not enough information was available to
2 make a clinical judgment.

3 As another example, 11 participants reported
4 allergy to an inactive ingredient, which in every
5 case was lactose intolerance. This does not
6 represent a true allergy that the label intends to
7 warn about. The OB/GYN panel classified those with
8 lactose intolerance as acceptable to use.

9 Further, there were 17 participants who
10 reported having some degree of intermenstrual
11 bleeding between periods prior to enrollment,
12 including some who FDA classified as selectors,
13 whom we did not, and some whom FDA classified as
14 not appropriate to use. The independent physician
15 panel assessed those with intermenstrual bleeding
16 prior to enrollment as acceptable to use,
17 consistent with the CDC medical eligibility
18 criteria, which classifies unexplained vaginal
19 bleeding as a Category 2 condition, meaning that
20 benefits generally outweigh risks.

21 The rationale for the differences between
22 our assessment and FDA's for the other categories

1 are similar. As I've illustrated, it's clear that
2 many of these participants do not represent actual
3 selectors, and we feel that our classification
4 strategy better assesses the clinical implications
5 of the self-selection decisions. However, even
6 among all of the 67 participants who FDA classified
7 as selectors not appropriate to use, while some
8 would not derive benefit from using Opill, when
9 considering the CDC medical eligibility criteria
10 classifications, only one may have had some
11 clinically important risk because she had a history
12 of breast cancer and indicated that she would use
13 the product. Overall, this suggests that the DFL
14 is effective in mitigating clinical risk associated
15 with the self-selection decision.

16 So let's turn to the self-selection table
17 populated according to the protocol specified
18 approach. We used this classification to calculate
19 our study endpoints. This analysis yields a
20 primary endpoint measure, or the proportion who
21 made a correct selection decision, of 99 percent,
22 far exceeding the prespecified target threshold.

1 Performance was consistent among adolescents and
2 among participants with limited health literacy.
3 The secondary endpoint measure, or proportion of
4 those who should not use who made a correct
5 decision, was 84.6 percent.

6 Now I'd like to turn focus to the use of
7 Opill in people with breast cancer. The warning
8 against the use of Opill in this population arises
9 from a concern that reproductive hormones may
10 increase the likelihood of recurrence or accelerate
11 recurrence in people with certain cancers, most
12 importantly, breast cancer.

13 The DFL, which we used in the ACCESS study,
14 included a broad warning, "Do not use if you ever
15 had any cancer." After the ACCESS study, this
16 statement was modified to be a more specific
17 warning based on experience in ACCESS and feedback
18 from FDA, namely, "Do not use if you have or ever
19 had breast cancer." The more general cancer
20 warning was moved to the, "Ask a doctor before use"
21 section.

22 Given the low prevalence of breast cancer in

1 women of reproductive age, it was not surprising
2 that there were only two women with breast cancer
3 in ACCESS; therefore, because of the label change,
4 and in the interest of testing this warning in a
5 sufficient sample of women with a history of breast
6 cancer, we conducted a targeted self-selection
7 study. The warning tested in this targeted
8 self-selection study is the warning appearing on
9 the final proposed Opill label.

10 In this study of over 200 women with a
11 history of breast cancer, 97 percent correctly
12 determined that Opill was not appropriate for their
13 use. The FDA has presented additional analyses of
14 this study making worst-case assumptions, but which
15 still support the ultimate conclusion that the
16 breast cancer warning on the Drug Facts Label
17 successfully mitigates risk that this small subset
18 of the potential OTC population would select to use
19 Opill. Overall, data demonstrate that the DFL
20 guides appropriate self-selection.

21 In conclusion, Opill has few
22 contraindications or other conditions necessary for

1 use. Furthermore, the proposed label guides
2 appropriate self-selection, including among women
3 with current or past breast cancer, and is
4 effective mitigating the clinical risk associated
5 with the selection decision.

6 I'll now turn to Dr. Goodwin for her
7 clinical perspective on this topic.

8 **Applicant Presentation - Pamela Goodwin**

9 DR. GOODWIN: Thank you, Dr. Bradford, and
10 hello. My name is Pamela Goodwin. I'm a breast
11 cancer medical oncologist and clinical
12 epidemiologist at Sinai Health System in Toronto,
13 senior scientist at the Lunenfeld-Tanenbaum
14 Research Institute, and a professor of medicine at
15 the University of Toronto. Today, I'm here to
16 provide my clinical interpretation of the potential
17 risk associated with the use of POPs in breast
18 cancer survivors.

19 The use of Opill is contraindicated in women
20 who have ever had breast cancer because of concerns
21 that breast cancer growth would be stimulated. The
22 concern arises mainly from preclinical research.

1 Clinical studies have shown an increased risk of
2 recurrence in postmenopausal breast cancer
3 survivors using estrogen; however, the clinical
4 evidence with progestin alone is more limited. Let
5 me briefly discuss the evidence we do have.

6 There is only one study that looks at the
7 impact of hormonal contraceptives on recurrence in
8 breast cancer survivors. This study was conducted
9 in the U.S., and it involved 1370 women, 97 of whom
10 had used hormonal contraceptives, only eight of
11 whom used POPs.

12 In the full study population, there were
13 92 breast cancer recurrences. Among the women who
14 used hormonal contraceptives, 6.2 percent had
15 recurrences. Among the women who did not use
16 hormonal contraceptives, 6.8 percent had
17 recurrences. This is a non-significant difference
18 with a p-value of 0.83. Additionally, there was no
19 difference in all-cause mortality in this study.
20 These data suggest that POPs may not impact breast
21 cancer recurrence.

22 There is a handful of additional small

1 studies of the impact of intrauterine
2 levonorgestrel in breast cancer survivors that has
3 provided similar results; however, with this small
4 evidence base, it's difficult to draw conclusions
5 regarding the potential impact of POPs on breast
6 cancer outcomes. Importantly, there are no
7 randomized data.

8 So how do clinicians deal with this
9 situation in clinical practice? First, it's
10 important to remember that all patients with breast
11 cancer are under the ongoing care of a physician.
12 Out of an abundance of caution, these patients are
13 routinely told by their physicians not to take
14 hormonal agents, including oral contraceptives, at
15 any time after breast cancer diagnosis. This
16 recommendation is reinforced by the
17 contraindication to Opill use by breast cancer
18 survivors on the Opill label.

19 When considering this aspect of the label,
20 it's important to recognize that any potential
21 concern about the use of POPs is not relevant to
22 all breast cancer survivors, but only to the subset

1 of patients who are interested in contraception, so
2 let's look at who these patients are. We know that
3 the majority of breast cancer patients are over the
4 age of 50 at diagnosis; 20 to 25 percent of all
5 breast cancer patients are diagnosed under the age
6 of 50, and of that group, a recent study found that
7 only 40 percent desired contraception, which
8 represents about 10 percent of all breast cancer
9 patients. Of that group, three-quarters are
10 currently using copper IUDs.

11 So this leaves a small but important subset:
12 approximately 2.5 percent of all breast cancer
13 patients who are interested in contraception but
14 not using IUDs, who might potentially be interested
15 in using an oral contraceptive such as Opill.

16 So how do I view the data you've seen on
17 Opill use in the context of the breast cancer
18 population? The current label includes two
19 statements about cancer, as you can see on this
20 slide. Both statements could be relevant to the
21 breast cancer survivor when making a decision about
22 Opill use, and both are important in the general

1 population in reaching the correct decision.

2 You've just heard the results of the
3 targeted breast cancer selection-study. In that
4 study, the sponsor scored subjects of making a
5 correct decision about Opill use when they used
6 either of the two statements in the label in their
7 decision making; that is they would either not use
8 Opill after reading the label or they would speak
9 to their physician before using Opill. This
10 resulted in a correct response rate of 97 percent.

11 The FDA focused on the statement in the
12 label, "Do not use if you have or ever had breast
13 cancer" to score responses as correct, excluding
14 individuals who would have talked to their doctors
15 before use or who had already talked to their
16 doctors about the use of oral contraception. Using
17 this approach, the FDA calculated that 95 percent
18 of breast cancer patients responded correctly. In
19 my opinion, both of these estimates of correct
20 responses are very good. Furthermore, in the small
21 group of patients who incorrectly selected Opill, I
22 believe this would likely be recognized and

1 addressed at follow-up visits with their
2 physicians.

3 As a breast cancer oncologist, I am strongly
4 supportive of the contraindication that women who
5 have or have ever had breast cancer should not use
6 Opill due to the very limited clinical data
7 regarding safety. From a clinical perspective, the
8 key consideration is that breast cancer survivors
9 make the correct decision not to take Opill
10 regardless of which component of the label guides
11 them.

12 I'm reassured that 97 percent of breast
13 cancer survivors made the correct decision not to
14 select Opill, particularly in the context of
15 real-world data from three studies in the U.S. and
16 Europe, showing that 3 to 7 percent of breast
17 cancer survivors are prescribed hormonal
18 contraception after diagnosis. Thus, I do believe
19 that the DFL guides breast cancer survivors to the
20 correct decision.

21 Although as a medical oncologist I always
22 want to minimize any risk to my breast cancer

1 patients, I also feel that any potential risk to
2 breast cancer survivors who incorrectly decide to
3 use Opill needs to be balanced against the
4 potential benefits of OTC access to Opill in the
5 larger population of women without breast cancer.
6 I'm comfortable that the risk to the overall
7 population is likely to be low.

8 I'll now turn the presentation over to
9 Dr. Laurora.

10 **Applicant Presentation - Irene Laurora**

11 DR. LAURORA: Thank you, Dr. Goodwin.

12 I'm Irene Laurora, senior director of
13 scientific affairs at HRA Perrigo. I have 30 years
14 of experience in the pharmaceutical industry,
15 having responsibility for strategic planning and
16 implementation of global clinical development
17 programs and for medical and scientific affairs
18 functions. Today, I will review the results of the
19 ACCESS Actual Use study to demonstrate that people
20 can use Opill appropriately, guided by the OTC
21 label.

22 In the ACCESS actual use phase, we assess

1 whether consumers follow the instructions and
2 directions when using and stop use and talk to a
3 doctor sections of the label. The ACCESS study
4 user population included 883 women with diversity
5 of age, education, income, race, and ethnicity.
6 Subpopulations of interest, including adolescents
7 and participants with low health literacy, were
8 well represented with sample sizes sufficient for
9 assessment of adherence. In fact, adolescents were
10 overrepresented, as we met targets for adolescent
11 enrollment as requested by FDA.

12 Of note, 80 percent of all participants were
13 using the least effective methods or no method of
14 contraception prior to enrollment, and 60 percent
15 of those under age of 18 reported using no method
16 of contraception. This is important because it
17 provides perspective to consider the potential
18 incremental clinical benefit in the OTC setting for
19 women who may choose Opill, as those in ACCESS did.

20 The proposed Drug Facts Label has very
21 simple directions, to take one tablet at the same
22 time every day. The label also provides

1 instructions for the occasions on what to do if a
2 pill is taken more than 3 hours late, commonly
3 referred to as a 3-hour window, or if a pill is
4 missed. In these cases, the label directs the
5 consumer to use a condom or other barrier method if
6 they have sex during the next 2 days. We term
7 these mitigating behaviors, as they are intended to
8 decrease the risk of pregnancy. Adherence to daily
9 pill taking is critical, and as you will see,
10 ACCESS demonstrated that people can take the pill
11 as directed.

12 Our goal was to achieve a level of adherence
13 similar to that seen in real-world prescription
14 oral contraceptive use. Thus, to determine the
15 appropriate threshold for acceptable adherence in
16 an OTC setting, we looked at typical adherence with
17 oral contraceptives in the prescription setting.
18 As you heard from Dr. Westhoff, studies using
19 prospective daily diaries showed that approximately
20 15 percent of participants miss taking 15 percent
21 or more of their active pills per pack. This means
22 that 85 percent of women will take about 85 percent

1 of their active pills, providing a target for
2 ACCESS adherence.

3 With that background, we set out to evaluate
4 whether adherence would be meaningfully adversely
5 impacted by making this product OTC. Let me remind
6 you about how we use these thresholds to inform our
7 decision making. In an actual use study, we are
8 measuring how often a behavior happened, but keep
9 in mind that what's most important is the clinical
10 impact of any behavior within the benefit-risk
11 framework.

12 Let's look at the first daily adherence
13 measure. The primary endpoint was a percent of
14 study days where Opill was taken. The target
15 threshold was set at 85 percent. In addition, we
16 prespecified a corresponding secondary endpoint.
17 This endpoint also included measuring clinically
18 important mitigating behaviors such as abstaining
19 from sex or using a barrier method of contraception
20 for the 2 days following a missed pill as directed
21 by the label.

22 We did not ask those 17 years or younger to

1 report on their sexual activity for two reasons:
2 first, daily sexual activity was not necessary to
3 calculate our primary endpoint; and second, we were
4 concerned that requiring daily reporting of sexual
5 activity might be a barrier to enrollment for
6 adolescents.

7 Overall, ACCESS demonstrated that the DFL
8 guides people to correctly take Opill every day.
9 Adherence to the instructions to take Opill every
10 day was assessed in 883 female participants who
11 provided information on over 90,000 days of use.
12 Participants reported taking Opill 92.5 percent of
13 days overall. This level of adherence was
14 consistent across important subgroups, and we have
15 highlighted for you those subgroups of participants
16 with low health literacy and those 12 to 14 or
17 15 to 17 years old. In addition, the secondary
18 endpoint shows that participants reported either
19 taking Opill or following label directions when
20 Opill was missed on 97 percent of days.

21 The next primary endpoint and its
22 corresponding secondary endpoint measured the

1 extent to which individual participants adhered to
2 daily pill intake over the course of their
3 participation in this study; so instead of looking
4 across the population, we are considering an
5 individual's performance over time.

6 Now let's break down these data.
7 84.6 percent of participants were adherent, meaning
8 that they reported taking Opill on at least
9 85 percent of days. The lower bound of the
10 confidence interval for this measure was
11 82 percent.

12 For subgroups of interest, performance was
13 generally consistent with the overall population,
14 noting the similar point estimates. After
15 considering mitigating actions, 95 percent of
16 participants reported either taking Opill or
17 following mitigating behaviors at least 85 percent
18 of the time, demonstrating that even in the
19 instance of missed pills, women follow the label
20 directions; again, which mitigate the clinical
21 risks associated with missed pills.

22 Importantly, we asked people why they missed

1 taking their pills, and we found that almost
2 60 percent of missed doses were reported to be due
3 to issues with obtaining contraceptive resupply.
4 Participants could be enrolled if they lived within
5 35 miles from a pharmacy site. The ability to
6 resupply was further restricted, as study staff had
7 to be present at the site. In fact, these resupply
8 issues, as well as the occasions that participants
9 did not have the pills with them, illustrate
10 precisely the barriers to adherence that could be
11 lessened by switching Opill to the OTC setting, and
12 as you heard from Dr. Westhoff, running out of
13 pills and not being able to get a resupply in a
14 timely manner is frequently reported as a reason
15 for non-adherence in the Rx setting.

16 Now let's turn to the endpoints measuring
17 adherence to pill intake at the same time each day.
18 This was assessed in two ways. In the primary
19 endpoint, we assessed whether participants took
20 their dose at approximately the same time of day as
21 the last dose they took, plus or minus 3 hours, and
22 in the secondary endpoint, we assessed whether they

1 took their dose no more than 27 hours after the
2 previous day's dose or chose appropriate mitigating
3 behaviors if the pill was taken late. This was
4 done to inform us whether participants would take
5 each daily dose no later than 3 hours after it was
6 due, which is a behavior thought to be needed to
7 maintain sufficient effectiveness.

8 We found that 96 percent of the time,
9 individuals reported correctly taking their dose
10 within 3 hours of their last reported dose, and
11 they reported taking Opill within 27 hours of the
12 prior day's dose or taking mitigating action
13 99 percent of the time. Subjects with low health
14 literacy and adolescents performed well and
15 consistent with the total population, thus
16 demonstrating that consumers are able to take Opill
17 at the same time every day.

18 Taken together, these primary adherence
19 endpoints evaluate two distinctly different
20 behaviors: taking a tablet every day and taking it
21 at the same time of day. To evaluate the
22 timeliness of dosing, we could only evaluate those

1 days when a dose was taken; thus, days when no dose
2 was taken were excluded from the analyses shown
3 here.

4 We understand that the full clinical benefit
5 is realized when these behaviors are performed
6 together; that is taking the pill every day within
7 the 3-hour window. FDA performed an analysis using
8 this construct. The analyses were referred to as
9 D-1 and D-2 in the FDA briefing material. These
10 analyses counted as correct days in which the
11 participant took a pill and that pill was taken
12 within the 3-hour window. This analysis found that
13 89 percent of the time, individuals reported
14 correctly taking their dose every day within
15 3 hours of their last dose and 74 percent of
16 participants took 85 percent or more of their daily
17 doses on time.

18 Mitigating behaviors are also important to
19 maintain clinical effectiveness. Let me share with
20 you this same analysis accounting for mitigating
21 behaviors. In this post hoc analysis, 93 percent
22 of the time, individuals reported correctly taking

1 their dose every day within 3 hours of their
2 previous day's dose or took appropriate mitigating
3 behaviors. And with regard to participant level
4 adherence, 83 percent of participants took
5 85 percent or more of their daily doses on time or
6 took appropriate mitigating behaviors, thereby
7 minimizing their risk of pregnancy.

8 Now let's turn to the participants who
9 reported taking Opill in their diaries, which was
10 incompatible with the amount of study drug
11 available to them. After the study was completed
12 and under review by FDA, it was noted that some
13 participants reported that they took Opill on more
14 days than was possible given the number of tablets
15 dispensed and/or returned. This is referred to as
16 overreporting in the sponsor briefing document and
17 improbable dosing by the FDA.

18 We defined overreporting as anyone who
19 reported in their diary at least one dose more than
20 the drug supply available to them, even if they had
21 used Opill for 6 months. This was a conservative
22 definition. Overreporting occurred in 261 of the

1 883 user participants. Actual use trials are
2 generally designed to capture a broad range of
3 possible behaviors and do not control participants'
4 behavior or their reporting of these behaviors, and
5 in these and other studies using self-reported
6 data, participants may report things that are not
7 possible.

8 HRA asked a qualified third party to
9 complete a comprehensive evaluation to understand
10 the situation, including a formal root cause
11 analysis. This independent company evaluated the
12 critical processes linked to both study planning
13 and study execution. Additionally, HRA conducted
14 several post hoc analyses and consulted experts in
15 the field of behavioral research and
16 self-reporting.

17 First, let me share the results of the
18 root cause analysis. The root cause analysis ruled
19 out several factors as root causes. This analysis
20 identified no systemic problems with the study
21 conduct, including the functioning of the e-diary
22 or investigational site, CRO, or sponsor-related

1 issue, but rather identified that some study
2 planning and execution elements might have
3 contributed to overreporting.

4 As you heard earlier, actual use studies are
5 different from typical controlled clinical trials.
6 Specifically, the study methodology needs to
7 capture participant behavior while minimizing
8 cueing. This is a delicate balancing act. As
9 related to study planning, the root causes
10 identified included the following: there were no
11 elements in place to prevent overreporting; the
12 design did not set out to identify when
13 participants were reporting taking more doses than
14 they could have taken; and the diary setup allowed
15 participants to continue to enter data into their
16 diaries specifically to allow them an opportunity
17 for resupply to capture breaks in pill-taking
18 behavior.

19 Regarding study execution, the preplanned
20 risk assessment, while conducted according to good
21 clinical practice, did not identify overreporting
22 as a significant risk, and overreporting was not

1 identified during the study, and therefore not
2 flagged as a protocol violation.

3 One potential causal factor that could not
4 be ruled out was the participant incentive. Paying
5 participants to complete a daily diary is standard
6 in the field. The incentive was constructed to
7 encourage diary completion but not to influence
8 pill-taking behaviors. Thus, the incentive was
9 paid regardless of whether participants entered yes
10 or no when asked if they had taken a pill.

11 In this study, as data were self-reported by
12 the participants themselves and with little
13 restrictions on reporting so as to capture a broad
14 range of possible patterns of use, participants
15 could report taking more drug than feasible. Some
16 participants may have made inadvertent data entry
17 mistakes, which might explain overreporting
18 observed in those participants who reported taking
19 a few excess doses. Approximately one-third of
20 overreporting participants reported no more than
21 20 percent excess doses compared to the number they
22 had access to. However, for the participants who

1 overreported to a large extent, it is most likely
2 that reporting of excess doses was deliberate.

3 The design elements in ACCESS that allowed
4 overreporting were necessary for two reasons: to
5 allow participants autonomy in decision making and
6 to minimize missing data. However, we understood
7 that some data from the participants who
8 overreported could not be reliably employed to
9 assess the adherence to Opill intake for those
10 participants; therefore, we conducted two
11 additional sensitivity analyses. The rationale for
12 those sensitivity analyses was to provide insight
13 into the potential impact of overreporting on the
14 interpretation of the ACCESS adherence results.
15 Let me review how these analyses were constructed,
16 the results, and finally our interpretation.

17 Recall that in the prespecified analysis, we
18 had 883 participants who reported on more than
19 90,000 days. This included 622 non-overreporters
20 with more than 61,000 of reported use and
21 261 overreporters with more than 29,000 days of
22 reported use. In our first post hoc sensitivity

1 analysis, we excluded all data from the
2 261 overreporters. This assumes the data provided
3 by the overreporters was non-informative of their
4 use of Opill at any time during the study.

5 Neither the root cause analysis nor our own
6 quality assurance activities have identified any
7 problems with diary reporting for those
8 participants that did not overreport. This
9 includes a robust population of 622 participants.
10 Interesting, we did find a precedent for this;
11 another actual use study for Oxytrol, a treatment
12 for overactive bladder that was approved for
13 Rx-to-OTC switch observed overreporting, however,
14 all participants who reported using 25 percent more
15 patch applications in their diary than were
16 purchased were excluded from their sensitivity
17 analysis. Ours is a more conservative approach, as
18 we considered even a single excess dose as
19 overreporting.

20 Let's look at the results of this analysis,
21 excluding overreporters. Here are the results for
22 the various primary adherence-related endpoints.

1 The prespecified analysis is highlighted in yellow
2 and the sensitivity analysis presented below. The
3 sensitivity analysis results across each endpoint
4 are very similar to the results of the prespecified
5 analysis. Each point estimate and a confidence
6 interval show that participants followed the label
7 directions.

8 In a second sensitivity analysis, we
9 included all participants in the user population
10 but censored their diary data after a revised stop
11 date. This revised stop date was defined as either
12 the date available drug supply would be exhausted
13 or the participants' last day of reported use in
14 the e-diary or to a nurse interviewer, whichever
15 came sooner. The strength of this analysis is that
16 it includes all data that is likely to be reliable.

17 This imputation assumes that the data
18 provided by all participants was accurate up until
19 the time they ran out of the drug or otherwise
20 indicated that they had stopped taking the
21 medication. This analysis included all
22 883 participants and about 56,000 days from the

1 non-overreporters and approximately 16,500 days
2 from the overreporters, but excluded the days of
3 reported use beyond the revised stop date.

4 Now let me show you the results. Again,
5 these results are very similar to the prespecified
6 analysis results highlighted in yellow and further
7 confirm the robustness of the data. Any
8 sensitivity analysis, especially post hoc
9 sensitivity analysis, should aim to capture the
10 range of possible outcomes. For each of the two
11 sensitivity analyses we just showed you, we
12 explained why we think they offer an appropriate
13 estimate of the target measurement.

14 Now let me take a moment to contrast these
15 analyses with the worst-case analysis presented in
16 the agency's briefing document. The agency created
17 a sensitivity analysis classifying all days for
18 overreporters as incorrect, indicating that they
19 did not take Opill on any use day. This analysis
20 adds a large number of incorrect days while
21 maintaining all use days reported by the
22 overreporters in the analysis.

1 If one assumes that participants did not
2 take Opill at any time, they would not meet the
3 study definition for inclusion in the user
4 population and would not contribute at all to the
5 analysis, and this scenario was already assessed in
6 another FDA analysis and in a sponsored sensitivity
7 analysis, number one, that excluded overreporters;
8 thus, a scenario that is completely improbable, and
9 that is to assume that all 261 women who reported
10 taking even one more pill than they had purchased
11 never took any [indiscernible] indication at all is
12 just not informative to the assessment of adherence
13 to Opill.

14 I'd like to now have Dr. Stone, an expert in
15 assessing self-reported data, discuss the
16 assessment of adherence in ACCESS with you.

17 **Applicant Presentation - Arthur Stone**

18 DR. STONE: Thank you, Dr. Laurora.

19 Good morning. My name is Arthur Stone. I'm
20 a clinical psychologist, and I've been involved in
21 diary and self-report research for over 45 years.
22 I am currently professor of psychology, economics,

1 and public policy at the University of Southern
2 California, where I also direct the Dornsife Center
3 for Self-Report Science. I'd like to say that I
4 had no role in designing or in the conduct of the
5 ACCESS study or in the initial analyses of the
6 data. I was asked to review the ACCESS trial and
7 the results, and to provide my thoughts on the
8 overreporting phenomenon seen in the trial and its
9 implications for the interpretation of these
10 results.

11 In my opinion, the ACCESS study meets or
12 exceeds the standards of most other studies
13 assessing adherence, including in oral
14 contraceptives. First, ACCESS used a time-stamped
15 electronic diary, a form of self-report that's
16 known to increase the accuracy of self-reporting
17 compared to more commonly used methods such as
18 retrospective questionnaires or paper diaries.
19 Second, ACCESS used a relatively short recall
20 period compared with published studies in oral
21 contraceptive work. Data could be retrospectively
22 reported for up to 11 days in ACCESS. This

1 contrasts with the typical retrospective reporting
2 designs for oral contraceptive studies that have
3 recall periods of up to 3 months or more.

4 Here are the data for all participants in
5 the user population, showing when they entered use
6 or non-use in their e-diaries. More than
7 80 percent of diary entries were made within 3 days
8 of the days participants were reporting on. These
9 data display the diary use for both non-
10 overreporters and for overreporters, and we see the
11 same pattern. Overall, extended recall was not
12 frequent, and it was no more frequent in
13 overreporters compared to non-overreporters;
14 therefore, there is no evidence that recall bias
15 contributed to overreporters.

16 While overreporting was observed in the
17 ACCESS study, I believe that the sponsor's
18 analyses, including the primary and sensitivity
19 analyses, present a clear and consistent picture of
20 adherence to Opill. Importantly, I do not believe
21 the overreporting observed in ACCESS undermines the
22 study's results for several important reasons.

1 First, self-reported adherence measures are the
2 standard and most common method for assessing
3 medication adherence in clinical research,
4 including studies of oral contraceptive use. Such
5 measures convey important information, although
6 it's well known that people make errors in
7 self-reporting, which can include overreporting of
8 adherence to medication.

9 Second, overreporting of the kind observed
10 in ACCESS occurs, but it is only detected in
11 studies when extraordinary design elements are
12 incorporated. These conditions are, first, that
13 study staff have information about participants'
14 medication supply and, second, the study allows
15 participants to report taking pills even when they
16 don't have pills available.

17 It's also important to note the design
18 elements in ACCESS that permitted overreporting
19 reflect a reasonable and frequently made compromise
20 to balance the need to minimize interference with
21 participant behaviors during the study, with the
22 ability to optimally collect the data in an actual

1 use trial. For example, minimization of missing
2 data is critical to the integrity of a 6-month
3 adherence study. HRA took prudent steps to
4 minimize missing data. Some of these steps allowed
5 overreporting to occur. Again, this reflected the
6 compromises made for an actual use trial design.

7 Now, the reasons as to why overreporting in
8 general occurs in medication adherence studies are
9 not clear, although several potential reasons have
10 been suggested in the literature. These include
11 the desire to stay in the study and the desire to
12 please the investigators. Similarly, the specific
13 reasons ACCESS participants overreported are not
14 known. In my view, the design of the ACCESS study
15 did not encourage overreporting; instead,
16 overreporting does appear to be a function of
17 decisions made by individual participants.
18 Furthermore, I do not think that it is plausible
19 that any language on the DFL could have contributed
20 to overreporting.

21 Let me now take a moment to share my
22 perspective on how overreporters' data have been

1 handled by the sponsor and by the FDA. Let's now
2 consider the entire data set in light of
3 overreporting. Nothing in the data set, and in my
4 own review, suggests the basis for questioning the
5 validity of the data reported by non-overreporters;
6 these are just how diary adherence data typically
7 look.

8 Sensitivity analyses can help understand the
9 impact of overreporting on the interpretation of
10 ACCESS. One reasonable approach is to exclude
11 overreporters from the analyses, as was done in the
12 first sensitivity analysis conducted by HRA and the
13 FDA. Another reasonable approach is to consider
14 data from all subjects as acceptable prior to the
15 point where they stopped using or ran out of drug,
16 which is what was assumed in the second sensitivity
17 analysis performed by the sponsor.

18 However, an analysis that imputes all
19 overreporters as totally non-adherent does not seem
20 reasonable. This is because it's just not sensible
21 to assume that when overreporters had pills, they
22 did not take any of them. In my opinion, the

1 totality of the evidence from ACCESS supports the
2 conclusion that participants were adequately
3 adherent to taking Opill.

4 Now, you've been asked by the FDA to think
5 about design considerations. Let me take a moment
6 to provide my perspective on the design elements
7 raised by the FDA. First, I would continue to use
8 an e-diary design as used in ACCESS to encourage
9 timely and accurate responding while minimizing
10 cueing. Given compromises necessary for a
11 long-term actual use trial, I would continue to
12 allow a degree of retrospective reporting to reduce
13 missing data.

14 As seen, the small amount of retrospective
15 reporting in ACCESS was effective in decreasing
16 missing data without contributing to overreporting.
17 I would use a similar compensation structure to
18 help minimize missing data. I would emphasize in
19 the diary training that compensation was based on
20 diary completion and not on pill taking. I might
21 also include a reminder of this in occasional text
22 messages.

1 To ensure comprehension of diary
2 instructions, I would be sure that participants
3 were observed using the e-diary during training,
4 and that's similar to what was done in ACCESS.
5 Unless there was a clear need to inquire about
6 doctor and healthcare professional contacts, I
7 would be reluctant to ask about this during the
8 course of a study, given the desire not to alter
9 usual health behaviors. Finally, I would attempt
10 to devise a way to know when pills were not
11 available for consumption in order to reduce the
12 possibility of overreporting. If it was possible
13 to know pill availability and to consider only
14 those diary reports when pills were available, then
15 the resulting adherence rates would be essentially
16 equivalent to those done by the sponsor in their
17 sensitivity analyses. Thus, while I might consider
18 some small design differences relative to the
19 ACCESS trial, these would not, in my opinion,
20 dramatically alter the adherence conclusions.

21 In summary, I believe the ACCESS study meets
22 or exceeds the standards of most oral contraceptive

1 adherence studies. The fact that there was
2 overreporting by some participants in ACCESS is
3 consistent with what is known about self-reported
4 adherence, although the particular type of
5 overreporting is rarely seen, as the conditions
6 detected are rare.

7 Overreporting also does not appear to be
8 impacted by the duration of recall nor undermine
9 the reliability of self-reporting of the other
10 participants. It is not a reason to treat all of
11 the data from the overreporters as totally
12 non-adherent, and it does not indicate that
13 confusion about the Drug Facts Label caused
14 overreporting.

15 So, after a review of the sponsor's and the
16 FDA's analyses, I believe that the ACCESS study
17 data are adequate to assess adherence to Opill
18 intake. I will now return the lectern to
19 Dr. Laurora.

20 **Applicant Presentation - Irene Laurora**

21 DR. LAURORA: Thank you, Dr. Stone.

22 Now that you've heard the adherence results

1 from ACCESS, let me address another of the FDA's
2 discussion questions. The FDA is asking you to
3 discuss whether the data support use in three
4 populations: all users, adolescents, and those
5 with limited literacy. I will review adherence
6 results in these populations. The FDA also asks
7 you to consider a fourth subpopulation, those
8 taking products, such as seizure medications, that
9 may interact with Opill and reduce its efficacy.
10 Of course, adherence in this population is
11 important, and we have no reason to believe it
12 would be different from the overall population.
13 However, effectiveness here is related to potential
14 changes in norgestrel exposure if a person would
15 select to use Opill or if these drugs were
16 initiated during use of Opill, and this will be
17 addressed later.

18 In yellow are the results of the general
19 population showing high adherence across all three
20 primary endpoints. With regard to adolescents, we
21 had sufficient representation of adolescents,
22 including those 12-to-14 years old, and most

1 importantly, they used Opill as directed, and they
2 performed consistent with the entire population
3 across all primary endpoints assessed.

4 Let me remind you that the need for
5 effective and accessible contraception in
6 adolescents is particularly urgent. Adolescents
7 face the most significant barriers to obtaining the
8 more effective contraceptive products, and
9 72 percent of their pregnancies are unintended.
10 Additionally, we had sufficient representation of
11 those with limited health literacy across the
12 development program, including 13 percent in the
13 ACCESS self-selection population and 14 percent in
14 the user population, and this is consistent with
15 the proportion of limited health literacy
16 population in the two most recent actual use
17 studies for products approved for Rx-to-OTC switch
18 by the FDA.

19 We sized the study such that the subgroups
20 of limited health literacy participants would be of
21 an absolute size sufficient to draw conclusions
22 about performance among those in that group and,

1 importantly, these participants performed
2 consistently as those in the entire population
3 across all primary endpoints assessed.

4 Overall, the totality of the evidence from
5 the ACCESS study is fully informative of potential
6 use in the OTC setting and demonstrates that women
7 adequately adhere to taking Opill in the OTC
8 setting, demonstrating that involvement of a
9 healthcare provider is not necessary to ensure good
10 adherence. This supports that women, including
11 adolescents and those with low health literacy,
12 would achieve the intended benefit in an OTC
13 setting.

14 I'll now turn the presentation over to
15 Dr. Sober.

16 **Applicant Presentation - Stephanie Sober**

17 DR. SOBER: Good morning. I'm Stephanie
18 Sober, global lead medical affairs, women's health,
19 for HRA Pharma/Perrigo, and a practicing
20 board-certified OB/GYN with fellowship training in
21 family planning. I would like to discuss some
22 considerations around effectiveness of POPs, and

1 put the adherence results in context, including in
2 light of the new pharmacodynamic insights obtained
3 from the Delayed Pill Intake Study.

4 There is a perception that POPs may not be
5 as effective as combined oral contraceptives. This
6 is based on data from the 1970s and early 1980s,
7 showing two things: first, that ovulation is less
8 suppressed in POP users than COC users, and second,
9 according to small pharmacokinetic studies, that
10 low serum levels of progestin remain after 24 hours
11 from intake.

12 The pharmacokinetic data was then
13 extrapolated to create the concept of the 3-hour
14 window; in other words, that missing a pill by more
15 than 3 hours could result in pregnancy, though this
16 is not based on any clinical efficacy data. To
17 provide additional evidence, we conducted the
18 Delayed Pill Intake Study, a prospective,
19 randomized, crossover, pharmacodynamic study, which
20 used modern investigative methods, including
21 ultrasound and serum hormone measurements.

22 The purpose of the study was to determine

1 the impact of Opill on cervical mucus and ovarian
2 activity during a treatment period of correct use
3 and after a deliberate delayed or missed pill. I
4 would like to discuss some of the FDA's comments on
5 the Delayed Pill Intake Study, particularly their
6 disagreement with the use of surrogate markers of
7 contraceptive effectiveness.

8 "A deliberate non-adherent study with
9 pregnancy as an endpoint is not feasible. Women
10 who don't want to get pregnant will not
11 deliberately miss pills. Women who do want to get
12 pregnant don't want to take pills. Both would be
13 unethical."

14 In the Delayed Pill Intake Study, we used
15 two well-characterized tools, the World Health
16 Organization's cervical mucus score and the
17 Hoogland score for ovarian function, to assess the
18 two widely accepted surrogates for potential
19 contraceptive efficacy, infertile cervical mucus,
20 and ovulation suppression. We recognize that
21 neither measure has been validated with pregnancy
22 as an endpoint, as this, too, would not be

1 feasible; however, both tools are widely used and
2 accepted.

3 For example, since 2008, PubMed lists
4 studies of nine different contraceptive methods,
5 two studies of the effect of obesity, and four on
6 drug-drug interactions on theoretical contraceptive
7 efficacy that employ the Hoogland score. This same
8 tool was also used in several pharmacodynamic
9 studies of deliberately missed COCs.

10 Let me share the key findings from the
11 Delayed Pill Intake Study, which has recently been
12 published in a U.S. peer-reviewed journal. First,
13 when used correctly, 67 percent of women did not
14 ovulate and another 10 percent ovulated with an
15 abnormal luteal phase likely not compatible with
16 pregnancy.

17 Thus, only 23 percent of subjects ovulated
18 with a normal luteal phase. This demonstrates that
19 ovulation inhibition and follicle growth
20 disturbance provide an important contribution to
21 Opill's mechanism of action; in fact, they likely
22 provide a larger contribution than previously

1 thought.

2 Second, when used correctly, fertile
3 cervical mucus was absent throughout the entire
4 cycle of use. So although approximately one-third
5 of users did ovulate during correct use, the
6 contraceptive effect is nonetheless maintained by
7 the hostile cervical mucus.

8 Third, when pill intake was delayed by
9 6 hours or missed altogether, neither the
10 percentage of women in whom ovulation was
11 suppressed, nor the frequency of fertile cervical
12 mucus, were significantly different from that
13 during correct use. This suggests Opill can be
14 expected to effectively protect against pregnancy,
15 even if a woman takes her daily pill late or misses
16 it entirely.

17 These data reassure us that the window for
18 maintaining efficacy if a pill is delayed or missed
19 is likely wider than previously thought. We
20 acknowledge that there are no data available to
21 assess the impact of missing more than one pill on
22 pregnancy risk. It is also not known how many

1 pills would need to be missed before contraceptive
2 efficacy is significantly reduced.

3 Even with these reassuring data, HRA has
4 maintained the 3-hour window language in the
5 proposed OTC label, and as you heard earlier, the
6 ACCESS study demonstrated excellent pill-taking
7 behavior. Ninety-seven percent of women either
8 took Opill daily as instructed or took appropriate
9 mitigating action if pills were missed. When women
10 did miss pills, in the majority of cases, 68
11 percent, it was a single missed day.

12 In light of the results from the Delayed
13 Pill Intake Study, the potential clinical
14 consequence of this small amount of non-adherence
15 in ACCESS, that is, risk of pregnancy, would be
16 expected to be further minimized.

17 Let's review the pregnancies observed in
18 ACCESS. As discussed previously, the primary focus
19 of the behavioral assessments in the ACCESS study
20 was related to the consistent daily use of Opill.
21 Because these behaviors are important to achieve
22 contraceptive effectiveness, ACCESS was not

1 designed as an efficacy study, but we did conduct
2 end-of-study pregnancy tests and recorded all
3 pregnancies reported during the study.

4 After review by the panel of independent
5 OB/GYNs, it was determined that among the
6 955 participants in the safety population, only
7 6 women got pregnant while using Opill. Of note,
8 the FDA's numbers differ slightly from ours due to
9 different time frames, as the FDA considers a
10 pregnancy on treatment even if conception occurred
11 in the 7 days after discontinuation. Regardless of
12 which numbers you use, pregnancies were uncommon
13 and in line with the typical use failure rate.

14 FDA noted some concerns about the impact of
15 body mass index on the effectiveness of Opill. The
16 available evidence suggests that effectiveness of
17 hormonal contraceptives is not affected by body
18 weight or BMI. A Cochrane review concluded that
19 the data did not indicate an association between
20 higher BMI, or weight, and effectiveness of
21 hormonal contraceptives. The CDC medical
22 eligibility criteria consider obesity to be

1 Category 1, meaning there are no restrictions for
2 POP use among women who are overweight or obese.

3 In addition, healthcare providers do not
4 prescribe a different dose regimen for hormonal
5 contraceptives, including POPs, to overweight or
6 obese women, and we have some additional data from
7 our development program. In the Delayed Pill
8 Intake Study, there was no difference in the effect
9 of deliberate non-adherence on cervical mucus or
10 ovarian activity in the subjects who were
11 overweight or obese compared with the normal weight
12 subjects.

13 In the ACCESS study, the distribution of BMI
14 was representative of that in the general U.S.
15 female population. Pregnancies were not
16 disproportionate in those with higher BMI. Thus,
17 the totality of the evidence supports the
18 effectiveness of Opill is not affected by weight or
19 BMI.

20 Turning now to a review of the actual use
21 results evaluating behaviors around when consumers
22 should take action during use and the potential

1 clinical impact, the proposed Opill Drug Facts
2 Label includes other information, directing women
3 on what to do during use of Opill. Statements
4 appear in the sections, "When using this product,
5 seek medical help right away and stop use, and ask
6 a doctor." Importantly, these ask-a-doctor events
7 can occur in any reproductive age women, but most
8 are not side effects of the POP and would not be
9 worsened by POP use. Thus, we evaluated these
10 behaviors as secondary endpoints in order to be
11 comprehensive in our assessment of consumer use.

12 As expected, given the inherent safety
13 profile of norgestrel, the situations in which
14 consumers should take action during Opill use were
15 uncommon in the ACCESS study. Unsurprisingly, in
16 many instances, the symptoms resolved
17 spontaneously, obviating the need to contact a
18 healthcare provider.

19 In the prescription setting, clinicians do
20 not routinely advise POP users of these
21 ask-a-doctor scenario, so, in fact, the Opill label
22 provides more information than does a prescribing

1 clinician. Importantly, users of oral
2 contraceptives have to make the same decisions
3 during their actual use, regardless of whether the
4 POP is obtained by prescription or OTC, and as
5 Dr. Westhoff told you, often providers do not see
6 women for up to a year after the initial
7 prescription.

8 Overall, the data showed no signal of
9 concern for use in the OTC setting and,
10 reassuringly, data from the final pivotal label
11 comprehension study do show that consumers
12 understand these key messages.

13 To summarize, our consumer studies show that
14 women of all reproductive ages can safely use Opill
15 in the OTC setting. Across two pivotal studies,
16 women were able to appropriately self-select
17 whether Opill was right for them and follow the
18 label instructions to guide use. Data from the
19 ACCESS study demonstrated that the Drug Facts Label
20 is sufficient to guide women to correctly take
21 Opill every day. There was high adherence to
22 taking the pill every day at the same time, and few

1 pregnancies occurred.

2 Given the inherent safety profile of
3 norgestrel, situations in which Opill users need to
4 consult a healthcare provider, take a pregnancy
5 test, and/or stop use in response to certain new
6 symptoms, are all uncommon and no different than
7 what patients face in the prescription setting.
8 Overall, the proposed Drug Facts Label contains all
9 the information needed to select and use Opill
10 safely and effectively, without incremental
11 clinical risk, making Opill appropriate for OTC
12 use.

13 Thank you, and I'll now turn the
14 presentation over to Dr. Glasier.

15 **Applicant Presentation - Anna Glasier**

16 DR. GLASIER: Good morning, everyone. My
17 name is Anna Glasier, a professor at the
18 Universities of Edinburgh and London and a
19 gynecologist by training. I have over
20 250 publications in peer-reviewed journals, most of
21 them on contraception. I have many years of
22 experience of running a large family planning

1 service in Edinburgh, and I have recently been
2 appointed by the Scottish government as their first
3 women's health champion. Today, you are being
4 asked to discuss a number of issues and to vote on
5 whether the data supports that Opill should be
6 available over the counter. To close the
7 presentation, I want to bring us back to the
8 clinical context and remind you why we are here
9 today.

10 Let me show you the pie chart that
11 Dr. Westhoff presented earlier, showing the
12 contraceptive method mix of U.S. women, age
13 15 to 49, at risk of pregnancy, with 61 percent of
14 them using the moderately or most effective
15 methods, and now you see the contraceptive method
16 mix among the ACCESS user population before
17 enrollment. In this population, 80 percent of
18 women, including the adolescents, were using either
19 no method or the less effective contraceptive
20 methods, and it was these women who chose to buy
21 Opill over the counter, and these women who would
22 arguably most benefit from OTC access to effective

1 contraception.

2 So we are here today because each year in
3 the United States, there are almost two- and
4 three-quarter million unintended pregnancies, most
5 of which could have been prevented by effective
6 contraception.

7 Progestin-only pills were approved in the
8 U.S. more than 50 years ago. It is true that the
9 clinical effectiveness trials on which approval of
10 the early POPs were based were not conducted to the
11 same rigorous standards used today, but this is
12 true for many medicines; and it is true that POPs
13 have stood the test of time. They have been used
14 by many millions of women around the world,
15 including women with contraindications to estrogen,
16 and therefore with relative contraindications to
17 pregnancy. If POPs were not effective, we would
18 surely know by now.

19 Clinicians have been advocating for oral
20 contraception to be available OTC for a very long
21 time. Thirty years ago, in 1993, in an editorial
22 in the international medical journal, *The Lancet*,

1 the author opened by saying that the oral
2 contraceptive pill had helped women, quote, "escape
3 from the confines of their own reproductive system,
4 but that these ex-prisoners remain on probation,"
5 unquote, because they still needed to see a doctor
6 regularly for a repeat prescription. And you've
7 heard today that key U.S. medical organizations,
8 whose members have considerable expertise in
9 contraception, formally support OTC access to oral
10 contraceptive pills.

11 Ultimately, for approval of Opill over the
12 counter, we need to establish that the incremental
13 benefits of having Opill available without seeing a
14 doctor outweigh the potential incremental risks, so
15 let me start with those potential risks.

16 There are three issues, and it's these that
17 you've been asked to vote on today. The first is
18 the risk of contraceptive failure due to inadequate
19 adherence. Adherence in the ACCESS study was not
20 different from published evidence on adherence to
21 oral contraceptives in the prescription setting.

22 Let's face it, the instructions for Opill

1 use are extremely simple; take one pill at the same
2 time every day. And in ACCESS, the vast majority
3 of women did just that, and if they made a mistake,
4 most took the appropriate mitigating action. And
5 let's remember that the women who did miss pills
6 often did so because they could only get a supply
7 from the site where they had enrolled, while in the
8 real-world situation, they could have bought Opill
9 from any drugstore. Finally, while ACCESS was
10 never intended as an effectiveness study, the
11 number of pregnancies was in line with the accepted
12 failure rate for typical use.

13 The second issue is safe use. Will women
14 use an over-the-counter POP any less safely than
15 they would use a prescription POP? The label
16 advises women to see a doctor if certain medical
17 situations arise during use. Dr. Sober has told
18 you that in the ACCESS study, these situations were
19 uncommon. She also told you that users of
20 prescribed oral contraceptives have to make exactly
21 the same decisions about what to do when these
22 situations arise during use.

1 Actually, all women of reproductive age have
2 to make the same decisions. Abnormal vaginal
3 bleeding is extremely common. Usually it resolves
4 spontaneously, and most women wait for that to
5 happen and don't go and see a doctor about it. We
6 don't worry that women using a progestin-only
7 contraceptive implant, or IUD, who do not need to
8 see a doctor for 3 and 5 years, respectively, for
9 contraception will come to harm because they may
10 not see a doctor about an episode of abnormal
11 vaginal bleeding, so let's not hold women hostage
12 to having to see a doctor to get this extremely
13 safe and effective POP because they don't go and
14 see one every time they have an episode of abnormal
15 vaginal bleeding.

16 So for me, the only incremental risk is
17 enabling women to self-select. Will women who
18 should not use Opill correctly choose not to use
19 it? For this, the FDA has raised four populations
20 of concern: women with breast cancer; women with
21 vaginal bleeding; and women using another hormonal
22 contraceptive or a concomitant product, which may

1 jeopardize efficacy of Opill.

2 Data the sponsor has presented today show
3 that there is a potential risk that a small number
4 of women who should not use Opill might do so were
5 it available over the counter. Most of these
6 people, subfertile women for example, will come to
7 no harm from using Opill. A very small number of
8 women with breast cancer may use Opill despite not
9 being eligible; however, Dr. Goodwin told you that
10 very few women with breast cancer are likely even
11 to consider using oral contraception, and in the
12 targeted breast cancer self-selection study, almost
13 all of them reached the correct decision not to use
14 it.

15 As for the women who reported unexplained
16 vaginal bleeding before selecting Opill, let's
17 remember that at enrollment, they had not been to
18 see a doctor. Like so many women, they were
19 already self-managing a very common condition, but
20 some may be prompted by the Opill label to go and
21 see a doctor. While it's unlikely that women on
22 seizure medication would purchase Opill, it's

1 important to note that both the label comprehension
2 studies and the self-selection data from the
3 program reassure us that the OTC proposed labeling
4 is effective in mitigating risks.

5 In ACCESS, there were 11 participants who
6 used Opill in combination with another hormonal
7 contraceptive, mostly longer acting methods like
8 injection, implant, or IUD. While these
9 participants would not receive incremental benefit
10 by use of Opill, overlapping use of this type would
11 not be associated with safety concerns.

12 Now, for the incremental benefits, there can
13 be no doubt that individual women would benefit
14 from having easier access and reduce barriers to
15 effective contraception, and this will provide
16 women with more effective choices and more autonomy
17 in deciding if and when to plan a family, and
18 ultimately, it will help prevent unintended
19 pregnancies and their social, economic, and health
20 consequences.

21 This is critical because each year in the
22 United States, maternal mortality is rising. Data

1 recently published by the CDC show an almost
2 90 percent increase in maternal mortality between
3 2018 and 2021, and this increases even higher when
4 looking at subgroups based on race. While we don't
5 know which of these pregnancies were unintended, we
6 can assume that many were. Regardless, with
7 advancements in medicine, these numbers should be
8 going down, not up.

9 When you vote on the FDA's questions, there
10 is one more risk I want to highlight, the risk that
11 faced with a wealth of data, you will lose sight of
12 the potential public health benefits of providing a
13 more effective contraceptive method over the
14 counter, so I want to remind you of those benefits.

15 Several groups have modeled the potential
16 impact of OTC availability on the rate of
17 unintended pregnancy using data from cohorts of
18 women who, when asked, expressed a theoretical
19 interest in an OTC pill. All of these studies show
20 a positive public health impact. However, we have
21 used data from the ACCESS study to model the
22 potential impact of an OTC POP on unintended

1 pregnancy, but the first time, our model, which was
2 recently published, incorporates characteristics of
3 a population of women who did actually purchase an
4 OTC POP, paying out of pocket to obtain better
5 contraception, and these women were sexually active
6 and at risk of pregnancy.

7 While we cannot know for certain how many
8 women might switch to Opill were it available OTC,
9 the model aims to estimate the impact among a
10 population of women who actually did so, and here
11 are the results.

12 If a cohort of 100,000 women, shown on the
13 left, continue to use the variety of methods with
14 different failure rates that the women were using
15 when they entered the ACCESS study, the estimated
16 number of pregnancies that would occur over one
17 year is 37,624. Compare this to the 7,000
18 unintended pregnancies expected in the right-hand
19 panel if these 100,000 women exclusively used OTC
20 POP for one year. This is an 81 percent reduction
21 in unintended pregnancies in one year in this
22 theoretical cohort of women.

1 It's important to point out that more than
2 90 percent of the 37-and-a-half-thousand
3 pregnancies that occurred in the left-hand panel
4 would occur among women using no contraception or
5 the less effective methods, and as discussed
6 earlier, it's these women with an unmet need for
7 effective contraception, and these women are the
8 most likely to buy Opill.

9 So let me finish by going back to the
10 beginning. The birth of the oral contraceptive
11 pill is considered one of the great milestones in
12 the history of medicine. We all know that the POP
13 is an extremely safe method of contraception. HRA
14 Pharma has demonstrated to you that the label does
15 work in guiding women to use Opill effectively, and
16 it's important to remember that women who need
17 contraception are not ill. They do not require a
18 diagnosis and they don't have a condition which
19 needs monitoring. In 2021, more than 1200 women in
20 the U.S. died from pregnancy-related causes. Not
21 all were unintended pregnancies, but somewhere, and
22 their deaths could have been prevented by

1 contraception.

2 Today, you're being asked to discuss a
3 number of issues and to vote on whether the data
4 support that Opill should be available OTC. Let's
5 make a little more history today and approve an
6 oral contraceptive pill over the counter. Thank
7 you for your time, and I will now turn the
8 presentation back to Dr. Laurora to address your
9 questions.

10 DR. COYLE: Thank you.

11 Before we take clarifying questions for HRA
12 Pharma, Dr. Espey, could you please introduce
13 yourself by stating your name and affiliation?

14 DR. ESPEY: Thanks. Good morning. My name
15 is Eve Espey. I am a professor of obstetrics and
16 gynecology, and chair of the department at the
17 University of New Mexico, and a complex family
18 planning subspecialist by training.

19 **Clarifying Questions**

20 DR. COYLE: Thank you.

21 We will now take clarifying questions for
22 HRA Pharma. Please use the raise-hand icon to

1 indicate that you have a question, and remember to
2 lower your hand by clicking the raise-hand icon
3 again after you have asked your question. When
4 acknowledged, please remember to state your name
5 for the record before you speak and direct your
6 question to a specific presenter, if you can. If
7 you wish for a specific slide to be displayed,
8 please let us know the slide number, if possible.

9 Finally it would be helpful to acknowledge
10 the end of your question with a thank you, and the
11 end of your follow-up question with, "That is all
12 for my questions," so that we can move on to the
13 next panel member. I might also suggest that we
14 limit our questions, offering them one at a time,
15 and then raising your hand for any additional
16 questions so that all have an opportunity to speak
17 in the time that we have available.

18 Okay. It looks like Dr. Armstrong. Go
19 ahead.

20 DR. ARMSTRONG: Thank you. This is Deb
21 Armstrong from Johns Hopkins. I have a couple of
22 questions specifically for Dr. Goodwin, and then a

1 couple for the applicant.

2 For Dr. Goodwin, is the Ostroot data broken
3 down by hormone receptor positive and negative
4 breast cancers? That's my first question. I
5 apologize. I don't have the slide number.

6 DR. LAURORA: Dr. Goodwin?

7 DR. GOODWIN: Pamela Goodwin. There was
8 simply a statement that the effects, the recurrence
9 rates, didn't differ by hormone receptor status,
10 but we don't have the actual numbers.

11 DR. ARMSTRONG: Thank you.

12 My second question for you, Dr. Goodwin, is
13 there data and/or concerns for the risks of the use
14 of progesterone-only pills in women with
15 potentially hormonally sensitive premalignant
16 lesions, such as atypical hyperplasia and in situ
17 cancers?

18 DR. GOODWIN: So you're talking about women
19 who don't yet have breast cancer and are at
20 potential risk for breast cancer. I can get you
21 that information after the break. I think the
22 strongest evidence we have is in people who have

1 BRCA mutations where there doesn't seem to be a
2 strong effect.

3 DR. ARMSTRONG: Thank you.

4 Then a couple of questions, more generally,
5 for the applicant. The first is, is Opill
6 available over the counter in any other countries?

7 DR. LAURORA: No. Opill is not currently
8 available in other countries, but some other
9 progestin-only contraceptives are.

10 DR. ARMSTRONG: Thank you.

11 There is lactose in Opill. Can you tell us
12 about whether -- I mean, obviously, that's a very
13 small amount -- there is documentation of the side
14 effects in the use of Opill in individuals who are
15 lactose intolerant?

16 DR. LAURORA: We don't have any reported
17 side effects from people who are lactose
18 intolerant, so we don't expect that that would be
19 an issue at all because there is a very tiny
20 amount.

21 DR. ARMSTRONG: Thank you.

22 And my final question, is there any

1 potential issues for women who might elect to
2 switch from a prescription combination oral
3 contraceptive to a POP if it became available over
4 the counter?

5 DR. LAURORA: We do not see any potential
6 issues with that. In fact, switching from a
7 combined oral contraceptive to Opill will be very
8 easy. You can start Opill on the very next day
9 after you stop taking your COC.

10 DR. ARMSTRONG: Thank you for answering my
11 questions. I'm done.

12 DR. COYLE: Thank you.

13 Ms. Robotti, please go ahead.

14 MS. ROBOTTI: Thank you. Suzanne Robotti.
15 I believe this will be for Russell Bradford. I'm
16 concerned at the representation of low literacy in
17 all of your trials. You noted the two earlier jobs
18 had 12 or 13 percent low literacy, and by that, I'm
19 sorry, you referred to two other FDA-approved
20 products that were switching from prescription to
21 OTC.

22 You mentioned that in those days, they had

1 12 or 13 percent low literacy participants, but the
2 naloxone studies, which were about 3 months ago,
3 had 33 percent limited literacy people in their
4 trial. In addition, the FDA, in my reading of
5 their documents, instructed you, the sponsor, to
6 include a minimum of 30 percent low literacy people
7 in your studies.

8 Low literacy can be measured in a couple of
9 ways, and you don't indicate how your studies
10 assess low literacy. However, including 30 percent
11 or more in your studies I don't believe should have
12 been an impossible challenge, given that something
13 around half of all Americans between the ages of 16
14 and 74 percent -- 16 and 74 years read below the
15 equivalent of a sixth grade level, according to the
16 U.S. Department of Education; actually, it's data
17 from the U.S. Department of Education. The U.S.
18 Department of Education itself says it's
19 21 percent, somewhere in there is a number.

20 Why did you not include a significantly
21 higher level of low literacy population? What were
22 your challenges?

1 DR. LAURORA: I'll ask Dr. Bradford to come
2 and address your questions. And, of course, in
3 ACCESS what we try to achieve is a sample that is
4 generated naturalistically in response to
5 advertising for this product, and what you saw
6 overall is the results of the ACCESS adherence data
7 demonstrate that subjects with low literacy can
8 take this product as directed, and it's very easy
9 directions for use; take one product every day.

10 Dr. Bradford?

11 DR BRADFORD: Russell Bradford from PEGUS
12 Research.

13 Ms. Robotti, let me first clarify that in
14 the naloxone studies, that was not an actual use
15 trial. That was a study that included a general
16 population recruited where enhancement for low
17 health literacy was possible; that is, screening
18 for low health literacy was potentially possible,
19 whereas Dr. Laurora mentioned, in an actual use
20 trial, these are participants responding to
21 advertisements who are interested in the product.
22 So what we find in these studies is typically a

1 proportion of low health literacy in the amount
2 that we saw here.

3 You mentioned also wondering about how we
4 assess for low health literacy. We use the REALM,
5 REALM-Teen, which is a test where participants are
6 asked to read and pronounce 66 health-related
7 words, and their literacy assessment is based on
8 how many of those words they pronounce correctly.
9 This is a test that's widely used in Rx-to-OTC
10 programs, but like every one of these rapid tests,
11 it certainly is limited and only evaluates one
12 component of literacy, indeed reading and
13 pronouncing words.

14 But I think to wrap that all up, what I'd
15 like to point out is that the proportion of low
16 health literacy is less important, in my view, than
17 the total number; that is, the total number, the
18 absolute size, of those low literacy groups were
19 appropriate in order to allow us to to draw
20 conclusions about how they perform.

21 MS. ROBOTTI: Thank you. That does answer
22 my question. I should point out I'm not a doctor.

1 Thank you.

2 DR. LAURORA: We definitely see a
3 significant public health need in people with low
4 health literacy to have access to safe and
5 effective contraception.

6 DR. COYLE: Thank you.

7 Dr. Shaw, please go ahead.

8 DR. SHAW: Yes, just unmuting. Thank you.
9 Pamela Shaw at the Kaiser Permanente Washington
10 Health Research Institute.

11 I'm sorry, I forgot the presenter, but my
12 question relates to slide 50 and then 52, which are
13 related, that had to do with the ACCESS results and
14 the differences between how people were counted. I
15 think you were explaining differences in that upper
16 left, 12 versus 67, but I'm a bit confused overall
17 about how many more people were labeled as
18 selectors by the FDA, 1550 versus selectors 1180,
19 and particularly how that impacts slide 52, which
20 is people who should not have used it. The FDA
21 found more people that were allergic that were
22 classified as selector.

1 I'm wondering -- I guess a two-part
2 question -- how did we get 1550 -- you understand
3 the differences -- versus the 1180? And maybe the
4 second part was, really, that slide 52 was all
5 about the differences between selectors and
6 non-selectors. Maybe I'll stop. What is the
7 difference in the FDA selector versus the selector?

8 DR. LAURORA: I'll have Dr. Bradford address
9 your questions.

10 DR. SHAW: Thank you.

11 DR. BRADFORD: Thank you. Russell Bradford.
12 Let me show slide CO-43 again, which shows our
13 strategy for classifying participants based on the
14 selection variable.

15 We take the input from both of these
16 questions as relevant to the selection decision.
17 As I mentioned, many times in response to the
18 self-selection question, we see participants give
19 responses that indicate that they don't quite
20 understand the context of the question. If, for
21 example, everyone universally understood the
22 question for how it's intended, it would be totally

1 reasonable to assume that their response adequately
2 categorizes them on selection versus non-selection,
3 but it's simply the case that they do not.

4 In many cases, I cited three examples, but
5 there are many cases in the data set and in our
6 experience that suggest that many people answer
7 this question in a more general sense. They like
8 the product. They think it's a nice product. They
9 think the labeling is nice. So they say yes as in,
10 "Oh, the hypothetical me might use this product if
11 it were on the shelf." When we asked the purchase
12 question and interpret their response to the
13 purchase question, it often adds a whole additional
14 layer of color, and our feeling is that a manual
15 review of the entirety of their response better
16 characterizes whether a participant actually
17 selects or not.

18 FDA's approach was simply to take the
19 response, okay or not okay, to that very first
20 question and assign selection on that basis. So
21 there's, as you note, a substantial difference in
22 how participants are classified, and we feel that

1 our approach better represents their actual
2 selection decision.

3 Let me show you now slide CO-52, which is
4 the slide that you referenced. In this case, among
5 those additional 55 that are shown there in the
6 right-hand column, 14 of those are added because
7 FDA categorized them from appropriate to use to not
8 appropriate to use. Those included three with a
9 history of cancer, one with liver problems, and 10
10 with pre-existing unexplained vaginal bleeding
11 between periods. The remaining 41 are those who
12 the FDA classified as selectors and who we
13 classified as non-selectors.

14 At the end of the day, however, I think, for
15 me, the important take-home message from this slide
16 is that in terms of actual clinical risk from
17 taking Opill, the single concern is participants
18 with a history of breast cancer, of which there
19 were one.

20 DR. LAURORA: I'd like to have Dr. Goodwin
21 also address your question.

22 DR. GOODWIN: Sorry. I was going to provide

1 the information that I had previously been asked by
2 Dr. Armstrong. There is some evidence that the use
3 of hormone replacement therapy, estrogen, in
4 postmenopausal women with atypical hyperplasia may
5 be associated with progression to breast cancer,
6 but we have not found any evidence that oral
7 contraceptives, or POPs in particular, are
8 associated with that risk of progression in
9 premenopausal women. I also want to point out that
10 my gynecologic colleagues have told me that these
11 high-risk breast cancer lesions are not considered
12 in the use of oral contraceptives when they're
13 given by prescription.

14 DR. COYLE: Dr. Shaw, does that address your
15 question?

16 DR. SHAW: Yes. Thanks. That addressed my
17 question. Thank you.

18 DR. COYLE: Okay. And I'll just add that
19 FDA is also prepared to discuss that issue of
20 selector versus non-selector in that analysis later
21 in the afternoon during the session.

22 DR. SHAW: Thank you.

1 DR. COYLE: I'll go ahead and call on
2 Dr. Baron.

3 DR. BARON: Thank you; just starting my
4 video. Hi. Thank you for all the presentations.
5 I have two questions.

6 DR. COYLE: Excuse me, Dr. Baron. I do need
7 you to state your name for the record.

8 DR. BARON: Oh, I'm sorry.

9 DR. COYLE: I apologize.

10 DR. BARON: Elma Baron from Case Western
11 Reserve University. I do have two questions. One
12 is a more general question, and the other one is
13 with regard to the breast cancer population as
14 well.

15 For the more general question, if Opill were
16 available as an over the counter and improving
17 access to more women, way more women, and younger
18 women, can somebody just speak towards any adverse
19 events or any anticipated side effects eventually
20 with the long-term use of Opill?

21 My second question with regard to the breast
22 cancer population, I think Dr. Goodwin excellently

1 showed that graph, that figure that showed the
2 percentage of breast cancer patients desiring oral
3 contraceptives, which is a very low percentage.
4 Given that is in the environment of oral
5 contraceptives being prescription and not over the
6 counter, I was just wondering if there's any
7 educated guesses as to whether once it's an
8 over-the-counter pill, that that percentage would
9 change; if that percentage would change? For
10 instance, would the percentage of those who are
11 currently using the copper IUD switch to the
12 over-the-counter oral contraceptives? If she could
13 just comment on that, that would be great. Thank
14 you.

15 DR. LAURORA: Okay. I'd like to ask
16 Dr. Glasier to address your question about
17 long-term use of contraceptives, as well as
18 Dr. Goodwin to discuss use in breast cancer.

19 DR. GLASIER: Thank you. Anna Glasier.
20 There are really no long-term risks of use of a
21 progestin-only pills, with a single
22 exception -- and I'm going to ask Dr. Goodwin to

1 address it -- of a small increase in the risk of
2 breast cancer, which is associated with both
3 long-term use of COCs and POPs. But before I hand
4 over to Dr. Goodwin, I'd just like to say that, of
5 course, that risk is the same whether women have a
6 POP or a COC prescribed to them than if they bought
7 a POP over the counter.

8 Dr. Goodwin, could you address the question
9 about breast cancer in women using a POP?

10 DR. GOODWIN: Right. I have two questions
11 to answer now. One is the issue of breast cancer
12 in women using POPs who don't already have breast
13 cancer, we know that there is a small increase in
14 risk. The relative risk is 1.2. That risk does
15 not vary when it's used over the counter or by
16 prescription, and I can provide some more
17 information about that.

18 Regarding your question about whether it is
19 likely breast cancer patients will switch from
20 copper IUDs or any other form of contraception to
21 over-the-counter POPs, I think that's highly
22 unlikely. The breast cancer population is very

1 focused on avoiding recurrence. They have been
2 cautioned by their physicians and will be cautioned
3 again by the label not to use this if they've ever
4 had breast cancer, so I am not concerned about that
5 particular risk.

6 Does that answer your question?

7 DR. BARON: Thank you.

8 DR. LAURORA: I'd also like Dr. Goodwin to
9 just simply address the trade-off of people who do
10 not have cancer and the potential for reducing
11 pregnancies.

12 DR. GOODWIN: Okay. So again, we're talking
13 about women who don't have cancer and what are the
14 potential breast cancer risks. I have just one
15 slide that I will show here. We know that the
16 relative risk, as I've already said, is about 1.2
17 regardless of whether POPs or COCs are over the
18 counter or by prescription. That has been
19 associated with an excess breast cancer risk in
20 women under 50, of 1 per 7,690 years of use or
21 roughly 13 cases per 100,000 person-years of use.

22 Given the current breast cancer survival

1 rates in the United States of 85 percent, that
2 translates to about two excess breast cancer deaths
3 per hundred thousand years of use. If we look at
4 the maternal death rates that you saw, that were
5 presented by Dr. Glasier, here I've taken maternal
6 death rates prior to the COVID pandemic. They're
7 actually higher now, but if we take maternal death
8 rates of 20 per 100,000 pregnancies and accept that
9 we can prevent 30,000 pregnancies per hundred
10 thousand years of use, we would avoid 7.5. maternal
11 deaths as opposed to having an excess of two breast
12 cancer deaths with every 100,000 years of use with
13 POP over-the counter or by prescription.

14 DR. COYLE: Thank you.

15 We'll go ahead and move on to
16 Dr. Walker-Harding, and please remember to state
17 your name, for the record.

18 DR. WALKER-HARDING: Hello. Leslie
19 Walker-Harding from the University of Washington.
20 I had a question. I know that this particular
21 company's progestin-only pill is not in other
22 countries, but there are other progestin-only pills

1 available to people over the counter.

2 Do you have any information on the safety
3 profile for women and adolescents that's been
4 published or available to evaluate for other
5 countries who have done this for a while?

6 DR. LAURORA: I'd like to have Dr. Guillard
7 address that for you.

8 DR. GUILLARD: Helene Guillard. Women
9 indeed are able to access oral contraception
10 without a prescription. It is in a number of
11 countries worldwide, around 100 countries. Since
12 2021, another progestin-only pill containing
13 another progestin, which is called desogestrel, is
14 also available without a prescription through
15 pharmacies in the United Kingdom. There is no
16 safety signal whatsoever about the use of POP
17 without a prescription in any of those countries.

18 DR. COYLE: Thank you.

19 Dr. Walker-Harding, did that address your
20 question?

21 DR. WALKER-HARDING: Yes, it did. Thank
22 you.

1 DR. COYLE: Thank you.

2 We'll move on to Dr. Curtis. Please state
3 your name for the record, and you can ask your
4 question.

5 DR. CURTIS: Thank you. Kate Curtis from
6 CDC. I've been trying to think about the
7 overreporting issue and how that affects our
8 interpretation of the results. If I'm correct, the
9 overreporters were identified by looking at those
10 who reported taking more pills than they had in
11 their supply, and the sensitivity analyses
12 addressed those and were generally reassuring.

13 But I'm wondering about if this
14 overreporting behavior was happening in this group,
15 it was likely also happening in the group that
16 wasn't identified as an overreporter. For example,
17 people who were missing pills or not taking pills
18 reported that they did, but that overreporting
19 didn't exceed their supply, so they weren't
20 identified as overreporters.

21 For the sponsor, I was wondering if there
22 had been any exploration about the validity of the

1 use data in those who were non-overreporters first,
2 and then also for Dr. Stone, you said pretty
3 clearly in a couple of your slides that from your
4 review, you didn't see any basis for questioning
5 the validity of those non-overreporters, and I was
6 just wondering if you could talk a little bit more
7 about what your review consisted of and how you
8 came to that conclusion.

9 DR. LAURORA: Yes. I'll address the issues
10 from the sponsor and have Dr. Stone address your
11 issues as well.

12 We conducted a thorough root cause analysis
13 and we hired an independent party to review all of
14 the data and all the processes in the study, and
15 they found nothing that would indicate that the
16 reporting by the non-overreporters was in any way
17 not consistent with what we should expect from
18 those people. We had no problems with a diary, and
19 we did extensive quality assurance review and found
20 no issues otherwise with the conduct of the study.

21 Dr. Stone?

22 DR. STONE: Yes. I understand the concern

1 about the overreporting. First, let me say that
2 this kind of overreporting is very rarely seen;
3 that you need those specific kind of conditions
4 where your people actually might not have pills,
5 and yet continue to have the ability to overreport.
6 Despite the rarity of those conditions, it has
7 occurred in the past. The Oxytrol trial was one
8 example, and there have been other examples.

9 The reason that I remain confident in the
10 ACCESS data is because when I look at the overall
11 conduct of the trial, the way it was set up, the
12 use of the electronic diary, the relatively short
13 reporting periods, I see nothing that raises a flag
14 for me that overreporting should be encouraged.
15 That's why I think that the data from the
16 non-overreporting group is especially reasonable
17 and would look like data from any other adherence
18 trial in this area. I just don't see anything that
19 would encourage overreporting in the
20 non-overreporting group.

21 DR. CURTIS: Thank you. And for the
22 sponsor, when you say quality control checks, I

1 guess, for all the participants, can you just
2 briefly talk about what that meant?

3 DR. LAURORA: Certainly. We audited
4 clinical study sites. We made sure before the
5 diary was employed that we did a significant amount
6 of testing to make sure it performed. We monitored
7 during performance, that it was performing well.
8 We had no complaints of performance by the
9 subjects, and we investigated the CRO and the
10 investigational sites, and found no problem.

11 DR. CURTIS: Thank you.

12 DR. COYLE: We will take Dr. Pisarik's
13 question, and that will conclude this session.

14 Dr. Pisarik, please state your name for the
15 record and direct your question to the sponsor.

16 DR. PISARIK: My name is Paul Pisarik from
17 Tulsa, Oklahoma. I just have a follow-up question
18 to two things that were brought up earlier. In
19 those countries in which the progestin-only pills
20 is over the counter, has there been any documented
21 decrease in the unintended pregnancy rates?

22 DR. LAURORA: I'd like to ask Dr. Glasier to

1 discuss that.

2 DR. GLASIER: So the quick answer is no. A
3 longer answer is that of course we have a national
4 health service in the United Kingdom, and all
5 contraception and all consultations for
6 contraception are free of charge. The women who
7 are buying a POP over the counter are tending to be
8 women who have run out of pills and who need a pill
9 in an emergency in the UK; and actually, it's too
10 soon to be able to see any effect on unintended
11 pregnancy rates because it only was approved over
12 the counter in July of 2021, so we don't have
13 enough data to look at unintended pregnancies.

14 DR. PISARIK: Thank you.

15 DR. COYLE: Thank you.

16 I do see that we have a few additional
17 questions. If we do have time later in our agenda,
18 we can go back to those, if possible; however, at
19 this time, to keep to our schedule, we will need
20 now to break for lunch. We will be reconvening at
21 1 p.m. Eastern Time.

22 Panel members, please remember that there

1 should be no chatting or discussion of the meeting
2 topics with other panel members during the lunch
3 break. Additionally, we would ask that you plan to
4 reconvene around 12:50 p.m. to ensure that you are
5 connected before the meeting reconvenes at 1 p.m.
6 Thank you.

7 (Whereupon, at 12:16 p.m., a lunch recess was
8 taken, and meeting resumed at 1:00 p.m.)
9
10
11
12
13
14
15
16
17
18
19
20
21
22

A F T E R N O O N S E S S I O N

(1:00 p.m.)

FDA Presentation - Pamela Horn

DR. HORN: Welcome back. Again, I'm Pamela Horn. I'm the director of the Division of Nonprescription Drugs II. I'm going to be providing an introduction to the FDA presentations before turning it over to my colleagues. The application we are discussing today, as you've heard, is a supplemental application to NDA 017031 for norgestrel tablet. If approved, this would represent the first prescription-to-nonprescription switch of a daily oral contraceptive in the U.S.

Norgestrel is a single ingredient pill containing a progestin. It has been approved for use in the prescription setting for the prevention of pregnancy in females of reproductive potential since 1973 and was last marketed in 2005. Marketing was stopped for business reasons and not for reasons of safety or effectiveness.

As we have heard this morning, unintended pregnancies are associated with many public health

1 effects, and improving effectiveness and access in
2 a real-world setting is an important public health
3 goal, where there is a lot of room for better
4 outcomes. There are many females of reproductive
5 potential in the U.S. who may wish to use a
6 contraceptive to prevent pregnancy, and thus, the
7 availability of oral contraceptives is a major
8 public health need, affecting a very large group of
9 stakeholders.

10 Currently, daily oral contraceptives are an
11 important part of the range of available
12 contraceptive options. In the prescription
13 setting, within which daily oral contraceptives are
14 currently available, available data indicate that
15 they are more effective than contraceptive methods
16 that are currently available without interaction
17 with a healthcare provider. FDA is asking the
18 joint committees to provide input on the likelihood
19 of safe and effective use in the target population
20 of consumers if the product were to be made
21 available without a prescription or interaction
22 with a provider and on the likelihood that

1 consumers that should not use the product, based on
2 the do-not-use messages in the proposed label, will
3 appropriately decide not to use the product.

4 As we ask the committee to consider these
5 issues, I want to provide a few general comments
6 about things FDA considers when determining whether
7 a product is suitable for the nonprescription
8 setting. Important among these considerations is
9 that the labeling that accompanies the product
10 provides enough information for consumers who would
11 consider using the product to determine if the
12 product is suitable for them to use; that they are
13 able to follow the directions for use on the Drug
14 Facts Label without assistance; and that they are
15 able to determine when to stop using the product
16 and when they should contact a healthcare provider
17 for assistance. In addition, it is important that
18 a product have a low potential for misuse and
19 abuse.

20 If an applicant with a product approved for
21 use in the prescription setting wishes to change
22 the approval to use in a nonprescription setting,

1 they need to provide information to FDA to support
2 that the benefits of the drug will still outweigh
3 the risks of the drug in a nonprescription setting,
4 where there is no learned intermediary to determine
5 whether the drug is suitable for an individual
6 patient or provide other advice or instructions.

7 As you will hear, there are unique
8 considerations for switching a drug to
9 nonprescription when instructions for use need to
10 be adhered to closely and on an ongoing basis to be
11 effective, and the consequences of not
12 understanding how to use it correctly could result
13 in unintended pregnancy.

14 Of note, unlike a prescription drug
15 approval, when a drug is approved for a switch to
16 nonprescription use, there is no mechanism for
17 approving it with a REMS to ensure that the
18 benefits outweigh the risks, and there is no third
19 behind-the-counter class of drugs in the U.S. like
20 there is in other countries, including examples
21 that were noted this morning. Drugs in the U.S.
22 are either nonprescription or prescription.

1 There is also no option for approving an
2 application with postmarketing requirements for the
3 applicant to conduct additional studies with the
4 goal of addressing remaining uncertainties about
5 the safety of a drug or to inform the need for
6 possible label changes. Finally, if one were to
7 decide that substantive changes would be needed to
8 the proposed labeling to support approval, they
9 would need to be tested in consumer behavior
10 studies prior to approval.

11 As you hear the FDA presentations, I'd like
12 you to keep in mind the following points. This
13 product is for the prevention of pregnancy, and
14 success or failure of a contraceptive is a binary
15 outcome. Either pregnancy is prevented or is not.
16 This product needs to be consistently used
17 correctly to prevent pregnancy, and we would like
18 the committee to consider, along with the potential
19 advantages of making this product available in a
20 nonprescription setting, the potential for
21 incorrect use of norgestrel tablet resulting in
22 unintended pregnancies based on the data submitted

1 to inform likely effectiveness.

2 As you consider these data, we would like
3 you to pay particular attention to the data in the
4 adolescent and limited literacy subpopulations. We
5 would also like you to consider the risks of
6 nonprescription availability to consumers who
7 should not use this product, such as consumers with
8 progestin-sensitive cancers, or consumers who
9 should talk to a healthcare provider before using,
10 such as consumers with abnormal vaginal bleeding of
11 undiagnosed etiology.

12 We are asking for your input to inform our
13 regulatory decision about this application. Thank
14 you for your assistance in discussing and
15 considering this important application, and I look
16 forward to hearing your opinions and insights.
17 Now, Dr. Anandi Kotak will talk about the efficacy
18 and safety of norgestrel tablet in the prescription
19 setting and its implications for the
20 nonprescription setting.

21 **FDA Presentation - Anandi Kotak**

22 DR. KOTAK: Good afternoon. My name is

1 Anandi Kotak. I'm a medical officer in the
2 Division of Urology, Obstetrics, and Gynecology.
3 Today, I will discuss the key efficacy and safety
4 findings that formed the basis for approval of
5 prescription norgestrel tablet, the knowledge we
6 have gained regarding norgestrel tablet and other
7 progestin-only contraceptives since the original
8 approval, and the implications of key concerns for
9 the nonprescription setting.

10 Before I begin, I would like to acknowledge
11 that FDA recognizes that sex and gender are
12 distinct terms, with sex defined as a biological
13 construct and gender as a social construct. FDA
14 understands that individuals self-identify by
15 gender, and for some, gender and sex are
16 concordant, while for others, they may not be
17 concordant. FDA also recognizes that individuals
18 may enroll in clinical trials based on gender;
19 however, contraceptive products are approved for
20 use on the basis of biological sex and reproductive
21 potential.

22 Therefore, in this presentation, I will

1 refer to contraceptive users according to the
2 currently approved prescription indication,
3 females, or females of reproductive potential, or
4 using gender neutral terms such as consumers,
5 individuals, or participants, to be as inclusive as
6 possible. Further discussion of this topic,
7 however, falls outside the scope of this meeting.

8 Before I continue, I would like to show some
9 examples of contraceptive methods for preventing
10 unintended pregnancy to clarify the topic of our AC
11 meeting. Emergency contraception can be employed
12 after unprotected intercourse, where the risk of an
13 unintended pregnancy is evident. Available
14 prescription contraceptive methods, such as
15 intrauterine systems -- also known as intrauterine
16 devices, or IUDs -- and subdermal implants are
17 examples of long-acting reversible methods of
18 pregnancy prevention, which are not dependent on
19 the user's adherence to dosing and administration
20 instructions and are among the most effective
21 methods of contraception available.

22 On the other hand, birth control pills,

1 transdermal systems, or patches, and vaginal rings
2 can be used longer or shorter term and are
3 dependent on user adherence to dosing instructions,
4 and are generally less effective than IUDs and
5 implants. Of the birth control pills, there are
6 two main types. One contains two hormones,
7 progestin plus estrogen, and the other type
8 contains one hormone, progestin only.

9 Our discussion today focuses on one type of
10 progestin-only pill, norgestrel tablet,
11 specifically for the indicated use of pregnancy
12 prevention in the nonprescription setting. In the
13 prescription setting, progestin-only pills are
14 prescribed in a highly selective population, namely
15 lactating females or in females who have
16 contraindications to estrogen., and this population
17 is generally highly motivated to use the product
18 correctly. On-demand methods, which include
19 barrier methods, are available over the counter and
20 are also options for individuals, but are generally
21 less effective than the prescription methods.

22 I will begin by reviewing the basis for the

1 original approval of prescription norgestrel
2 tablet, as well as the considerations for dosing
3 and administration, which are particularly relevant
4 for the nonprescription setting. I will then
5 discuss the estimation of effectiveness of
6 norgestrel tablet for the nonprescription setting,
7 followed by a review of key safety concerns for
8 norgestrel tablet and their implications for the
9 nonprescription setting. Finally, I will discuss
10 two key considerations for translating effective
11 and safe use of norgestrel tablet to the
12 nonprescription setting.

13 The efficacy and safety of norgestrel tablet
14 was established in 1973, at the time of the
15 original approval for prescription use.

16 Post-approval data from 1973 until 2005, as well as
17 knowledge we have gained from other progestin-only
18 contraceptives, also informed the safety profile of
19 norgestrel tablet. The efficacy data to support
20 approval came from eight clinical studies conducted
21 by the applicant in the United States. The Pearl
22 Index, the primary efficacy endpoint for

1 contraceptives which describes how well a
2 contraceptive product prevents unintended
3 pregnancy, was 2.3 per 100 woman-years. Exposure
4 in nearly 2200 study participants, over more than
5 20,000 treatment cycles, provided the safety data
6 to support approval of norgestrel tablet.

7 The dosing regimen evaluated in the clinical
8 trials to support approval was one tablet taken at
9 the same time every day. Of note, norgestrel
10 tablet was approved for use in all females of
11 reproductive potential, regardless of age, which
12 will be relevant in later discussions.

13 The following dosing and administration
14 instructions for norgestrel tablet, as described in
15 the approved prescription labeling, are critical
16 for pregnancy prevention. Take one tablet daily at
17 the same time each day; take a delayed or missed
18 tablet as soon as possible and continue with the
19 next dose at the usual time; and take norgestrel
20 tablet continuously with no break between packs,
21 even when vaginal bleeding is present. Use of
22 additional non-hormonal contraception, meaning

1 barrier methods such as condoms, is needed for the
2 next 48 hours when a tablet is taken three or more
3 hours late or missed, or when vomiting or diarrhea
4 occurs within 4 hours after taking the tablet.

5 I will now provide an overview of the
6 effectiveness of norgestrel tablet and the
7 implications for the nonprescription setting.
8 First, I will provide an overview of the primary
9 efficacy endpoint for contraceptives, the Pearl
10 Index, from the prescription setting.

11 I will then discuss the challenges of
12 estimating the effectiveness of norgestrel tablet
13 in the nonprescription setting in light of factors
14 affecting effectiveness, such as issues pertaining
15 to adherence to the recommended dosing regimen and
16 the changing population, and in light of the
17 available sources of data for estimating
18 effectiveness and the limitations therein. I will
19 also discuss remaining questions regarding the
20 effectiveness of norgestrel pertinent to the
21 nonprescription setting.

22 The Pearl Index is a technique used to

1 describe the primary efficacy endpoint of interest
2 for contraceptives and is used to demonstrate
3 effectiveness to support regulatory approval of
4 contraceptive products. Historically, the Pearl
5 Index has been used since the approval of the first
6 oral contraceptive product in 1960. The Pearl
7 Index predicts the number of females who are likely
8 to become pregnant during one continuous year of
9 using solely the contraceptive method under
10 investigation, and is usually reported as the
11 number of pregnancies out of a total of 100 women.

12 The formula for calculation of the Pearl
13 Index is shown here. In order to calculate the
14 Pearl Index to support approval of a new
15 contraceptive product, FDA requests documentation
16 of both on-treatment pregnancies and evaluable
17 cycles. On-treatment pregnancy is defined as a
18 pregnancy that occurs during use of the
19 contraceptive product under investigation. This
20 also includes a pregnancy that occurs within 7 days
21 of discontinuation of the product.

22 An evaluable cycle is defined as a cycle

1 where intercourse occurred and additional
2 non-hormonal, or backup, contraception such as
3 condoms, or emergency contraception, was not used.
4 A smaller or lower Pearl Index indicates higher
5 contraceptive efficacy or greater ability of the
6 product to prevent unintended pregnancy.

7 Methodologies differ between the analysis
8 used in the original approval in 1973 and current
9 FDA clinical trial recommendations for approval of
10 contraceptives. Namely, present-day calculation of
11 the Pearl Index includes only females up to age 35
12 and evaluable cycles. Females over the age of 35
13 have a decreased likelihood of becoming pregnant
14 and are therefore excluded from the efficacy
15 analysis. Similarly, non-evaluable cycles are
16 excluded from analysis because of the possibility
17 that pregnancy did not occur because the individual
18 was not truly at risk for pregnancy during that
19 cycle.

20 When considering the available data to
21 estimate effectiveness of norgestrel in the
22 nonprescription setting, we must also consider

1 factors that can affect the effectiveness of
2 norgestrel, including extrinsic factors, which are
3 modifiable, and intrinsic factors, which are not
4 modifiable. An example of an extrinsic factor that
5 may affect effectiveness of norgestrel is
6 adherence.

7 The contraceptive efficacy of norgestrel is
8 highly dependent on strict adherence to the dosing
9 regimen, and adherence is dependent on consumer
10 behavior. Therefore, it is reasonable to conclude
11 that consumer behavior can affect contraceptive
12 efficacy. Intrinsic factors on the other hand
13 include population characteristics such as body
14 mass index, the prevalence of which may change over
15 time in a population.

16 As previously mentioned, norgestrel tablet
17 should be taken daily at the same time each day to
18 prevent pregnancy. It is also critical to know
19 what to do when a tablet is delayed or missed, or
20 if vomiting or diarrhea occurs, and when to use
21 additional non-hormonal contraception.

22 The need for strict adherence to the daily

1 dosing regimen is best understood when considering
2 the pharmacokinetic and pharmacodynamic properties
3 of norgestrel and similar progestin-only pills.
4 Norgestrel demonstrates a short elimination
5 half-life, resulting in serum progestin levels that
6 are near baseline 24 hours after oral intake. In
7 addition, norgestrel demonstrates low steady-state
8 progestin levels and large variations in serum
9 levels among individual users.

10 In contrast, as previously mentioned,
11 combined oral contraceptives contain both a
12 progestin and estrogen component. This results in
13 reliable suppression of the mid-cycle LH and FSH
14 peaks and higher steady-state serum progestin
15 levels. As a result, COCs prevent pregnancy
16 primarily by suppressing ovulation, whereas
17 progestin-only pills such as norgestrel less
18 reliably suppress ovulation and also depend on
19 cervical mucus effects to prevent pregnancy. If
20 cervical mucus effects are not consistently
21 maintained when using POPs such as norgestrel, and
22 ovulation occurs during that cycle, pregnancy is

1 more likely, as sperm can survive in the female
2 reproductive tract for up to 5 days after
3 intercourse.

4 The applicant conducted Study 151042-002 to
5 evaluate the impact of a delayed or missed pill on
6 cervical mucus and ovarian activity. Of note, the
7 study was conducted voluntarily without FDA
8 feedback. The applicant states that there were no
9 differences in cervical mucus scores or ovarian
10 activity scores after a 6-hour delay or missed
11 tablet; however, cervical mucus and ovarian
12 activity scores are not primary measures for
13 contraceptive efficacy but may be supportive
14 evidence of contraceptive effect when considered
15 together with the Pearl Index from phase 3 trials.

16 In addition, the study lacks
17 generalizability, as a sample size of 50 would not
18 adequately capture the wide variations in serum
19 progesterin levels previously mentioned, and females
20 with BMI greater than 32 were excluded from
21 enrollment. In conclusion, Study 002 cannot
22 demonstrate that delayed intake of norgestrel

1 tablet does not alter the risk of unintended
2 pregnancy.

3 Changes in the characteristics of the
4 population since the 1970s may also impact the
5 effectiveness of norgestrel tablet today. The
6 prevalence of obesity in the United States has more
7 than tripled since 1960. This is especially
8 concerning, given that recent approvals of hormonal
9 contraceptives have shown that efficacy may be
10 decreased as much as 40 percent in females with
11 increasing BMI; however, the impact of obesity on
12 the efficacy of norgestrel tablet has not been
13 directly studied.

14 Available sources of data to inform
15 effectiveness of norgestrel tablet in the
16 nonprescription setting include the original
17 clinical trial data, published literature, and the
18 actual use study conducted by the applicant in
19 support of this application. As previously
20 discussed, the original clinical trial data
21 includes data generated from eight clinical studies
22 conducted to support the prescription approval of

1 norgestrel tablet in 1973. A limited number of
2 clinical studies have attempted to describe the
3 efficacy of norgestrel in the post-approval
4 prescription setting and are the basis for the
5 meta-analysis submitted by the applicant. The
6 ACCESS actual use study also generated data
7 regarding contraceptive efficacy; however, this was
8 not the primary purpose of the study.

9 The Pearl Index for norgestrel tablet as
10 derived from available sources of data is shown
11 here. For context, the Pearl Index for combined
12 oral contraceptive, approved around the same time
13 as norgestrel tablet in the early '70s, was
14 typically less than 1. As you can see, the Pearl
15 Index for norgestrel tablet is more than double
16 that of COCs, meaning norgestrel and other POPs are
17 less effective than COCs.

18 Neither the original clinical trials nor the
19 ACCESS AUS used methods of determining the PI that
20 are consistent with current standards. In
21 addition, the limitations of estimating the Pearl
22 Index previously discussed preclude comparisons

1 across available sources of data. Of note, these
2 estimates are not reflective of real-world
3 effectiveness of norgestrel tablet, and what is
4 known about real-world effectiveness is based on
5 the prescription setting.

6 The applicant conducted a meta-analysis of
7 published literature at FDA's request to provide a
8 current understanding of norgestrel's contraceptive
9 effectiveness in today's population. Limitations
10 of the applicant's methodology and interpretation
11 include the heterogeneity of study designs,
12 including differences between study populations and
13 sample sizes; lack of generalizability due to
14 differences in study populations and methods for
15 determination of a evaluable cycles; inconsistent
16 analysis methodologies between studies; varying
17 study durations, ranging from 6 months to 5 years;
18 as well as inclusion in some studies of lactating
19 females who are at decreased risk for pregnancy due
20 to anovulation, and are also a highly motivated
21 population.

22 In a supportive analysis of data from the

1 ACCESS AUS, the applicant reported a Pearl Index of
2 2.2 based on six on-treatment pregnancies, whereas
3 FDA's analysis of the Pearl Index is based on nine
4 on-treatment pregnancies. In addition, FDA's
5 analysis includes fewer cycles compared to the
6 applicant's analysis due to differences in the
7 derivation of exposure duration.

8 Two of the nine pregnancies occurred in
9 participants with a body mass index between 25 and
10 29.9 kilograms per meter squared, whereas three
11 pregnancies occurred in participants with BMI
12 greater than or equal to 30. The Centers for
13 Disease Control and Prevention define overweight as
14 a BMI greater than 25 but less than 30, and obesity
15 as a BMI greater than or equal to 30. Therefore,
16 slightly more than half of pregnancies occurred in
17 individuals with BMI in the overweight or obese
18 categories. Of note, pregnancies were not
19 stratified by body weight or BMI at the time of
20 original approval, precluding direct comparisons to
21 today's population.

22 As I previously mentioned, the ACCESS AUS

1 was not designed to assess contraceptive efficacy,
2 limiting interpretation of the Pearl Index.
3 Additional limitations of this analysis include the
4 following. First, the sample size of the study is
5 about one-third the size of a contraceptive
6 clinical trial for a new product, causing the Pearl
7 Index estimate to lack precision. Because of the
8 high discontinuation rate among study participants,
9 less than half of study participants in this 6-
10 month study completed and reported the results of
11 the end-of-study pregnancy test. There may have
12 been more pregnancies that were unreported.

13 In addition, the use of all menstrual
14 cycles, as opposed to evaluable cycles, produces a
15 larger denominator, causing the Pearl Index to
16 appear smaller than it may actually be. Because
17 sexual activity and sexual history data in
18 adolescents were not collected, the pregnancy risk
19 for these individuals is unknown, which may also
20 result in a larger denominator and a Pearl Index
21 that appears smaller. A smaller Pearl Index, as I
22 mentioned previously, may lead us to believe that

1 norgestrel tablet is more effective than it
2 actually is, and lastly, the phenomenon of
3 improbable dosing, to be discussed later today by
4 my colleagues, also limits interpretation of this
5 data.

6 In summary, the expected contraceptive
7 efficacy of norgestrel tablet as a nonprescription
8 product for prevention of pregnancy is unknown for
9 the reasons listed here. Real-world estimates of
10 the failure rate for oral contraceptives, another
11 way to think of the Pearl Index outside of the
12 research environment, range from 4 to 9 percent,
13 depending on the source of the data; however, these
14 estimates are primarily based on COCs.

15 Recall that the Pearl Index for COCs in the
16 1970s was less than 1. Because POPs account for
17 10 percent of oral contraceptive prescriptions in
18 the U.S., and because the Pearl Index for POPs may
19 be more than double that of COCs, as previously
20 discussed, it stands to reason that the failure
21 rate for real-world effectiveness of POPs, such as
22 norgestrel, may be quite a bit higher than

1 9 percent, meaning norgestrel may not be nearly as
2 effective as we might think out in the real world.

3 Although progestin-only contraceptives,
4 including norgestrel, are generally regarded as
5 safe, important safety concerns exist. In the
6 nonprescription setting, the absence of a learned
7 intermediary means that consumers must be able to
8 identify which safety concerns apply to them and
9 know what to do about them.

10 This section will begin with a review of the
11 known safety profile of prescription norgestrel
12 tablet, followed by a discussion of the primary
13 safety considerations for the nonprescription
14 setting, and then additional considerations for the
15 nonprescription setting.

16 The approved prescribing information for
17 norgestrel tablet, or Opill, updated in 2017, lists
18 the following contraindications: breast cancer or
19 other progestin-sensitive cancer now or in the
20 past; known or suspected pregnancy; abnormal
21 vaginal bleeding of undiagnosed etiology;
22 hypersensitivity to any component of the product;

1 and benign or malignant liver tumors. In addition,
2 the prescribing information describes warnings and
3 precautions for the conditions listed here. The
4 most clinically significant of these concerns
5 include ectopic pregnancy, a rare but serious
6 event; bleeding pattern alterations; and drug
7 interactions.

8 Considerations for the safe use of
9 norgestrel tablet in the nonprescription setting
10 include important safety concerns based on the
11 prescription label, as well as additional
12 considerations that would typically be conveyed by
13 a learned intermediary that may not be represented
14 in prescription labeling.

15 This discussion focuses on the most
16 significant safety concerns for this product,
17 including breast cancer and other
18 progestin-sensitive cancers, abnormal vaginal
19 bleeding of undiagnosed etiology, bleeding pattern
20 alterations, and drug interactions. Additionally,
21 we will discuss use in adolescents for whom the
22 prescription product is approved, the potential

1 impact of progestins on bone mineral density, and
2 current use of hormonal contraceptives or
3 intrauterine systems.

4 Use of progestin-containing contraceptives
5 such as norgestrel may increase the risk of
6 recurrence or stimulate the growth of an
7 undiagnosed progestin-sensitive tumor. Nonclinical
8 data demonstrates stimulated growth and metastasis
9 of breast cancer with exposure to progestins;
10 however, insufficient clinical data exists to
11 estimate the difference and relative risk of these
12 cancers with chronic norgestrel use.

13 Although breast cancer is the second most
14 common cancer among females in the United States,
15 it occurs rarely in females under the age of 50.
16 Other progestin-sensitive cancers such as melanoma,
17 meningioma, and adenocarcinoma of the lung are less
18 common than breast cancer in this demographic, but
19 do occur, as seen here.

20 Abnormal vaginal bleeding is defined by
21 relation to an individual's menstrual cycle and
22 refers to differences in the timing, quantity, or

1 duration of bleeding episodes. Abnormal vaginal
2 bleeding may differ from an individual's baseline
3 in timing by both the regularity and frequency of
4 bleeding, in quantity by increased volume, and
5 duration by lasting more days than usual menses or
6 longer than 8 days.

7 Many conditions can cause abnormal vaginal
8 bleeding, including structural or non-structural
9 causes, as well as pregnancy. Structural causes of
10 abnormal vaginal bleeding may include benign
11 conditions such as polyps or fibroids, or malignant
12 conditions, meaning cancer. Non-structural causes
13 may include disorders of coagulation, ovulatory
14 dysfunction, which can result from a variety of
15 endocrine abnormalities such as thyroid disorders,
16 or iatrogenic causes such as medications. Both
17 intrauterine and ectopic pregnancy can cause
18 abnormal vaginal bleeding as well.

19 Up to one-third of reproductive age females
20 will experience abnormal vaginal bleeding of some
21 kind in their lifetime, which accounts for nearly
22 30 percent of gynecology office visits annually.

1 Endometrial cancer is rare in this population,
2 however, initiating norgestrel use may delay the
3 diagnosis and treatment of the underlying cause of
4 abnormal vaginal bleeding.

5 Norgestrel use may also cause bleeding
6 pattern alterations, making it difficult to
7 distinguish between adverse effects of the drug
8 versus underlying pathology. With use of progestin
9 such as norgestrel, the absence of estrogen causes
10 thinning of the endometrium and disruption of
11 endometrial angiogenesis, thus producing irregular
12 and unpredictable bleeding, and sometimes the
13 absence of menstrual bleeding altogether. Frequent
14 irregular menses or absence of menstrual bleeding,
15 or amenorrhea, often cause discontinuation of
16 progestin-only contraceptives.

17 Alterations in bleeding patterns with
18 norgestrel use may potentially result in delayed
19 diagnosis and treatment of pregnancy, either
20 intrauterine or ectopic, which may require urgent
21 medical attention, or underlying causes of abnormal
22 vaginal bleeding that may arise during norgestrel

1 use such as polyps, fibroids, thyroid disorders, or
2 polycystic ovarian syndrome, but perhaps most
3 importantly may result in missed opportunities for
4 timely use of emergency contraception, as the
5 individual may not recognize the risk for
6 unintended pregnancy.

7 In summary, both abnormal vaginal bleeding
8 and bleeding pattern alterations with norgestrel
9 use may indicate conditions that require urgent
10 medical attention such as ectopic pregnancy or
11 miscarriage. Nonprescription use may increase
12 delayed evaluation by a healthcare provider or
13 missed opportunities to use emergency
14 contraception.

15 The questions that then remain are the
16 following:

17 Will individuals choosing norgestrel be able
18 to self-identify abnormal vaginal bleeding
19 requiring healthcare provider evaluation prior to
20 initiation?

21 Will individuals using norgestrel who
22 develop bleeding pattern alterations be able to

1 self-identify the presence of abnormal vaginal
2 bleeding that requires healthcare provider
3 evaluation?

4 Will individuals understand that the
5 bleeding profile with norgestrel use is not the
6 same as that with use of most COCs, and seek timely
7 care when abnormalities occur?

8 Drug interactions with norgestrel are
9 another important consideration for the
10 nonprescription setting due to the potential for
11 reduced contraceptive efficacy of norgestrel with
12 concomitant use of an interacting drug. Many drugs
13 and herbal products induce hepatic enzymes, such as
14 CYP3A4, increasing the metabolism of CYP3A4
15 substrates such as norgestrel. This in turn may
16 decrease contraceptive efficacy of norgestrel.
17 Conversely, norgestrel may also decrease the
18 efficacy of other drugs such as the emergency
19 contraceptive containing ulipristal acetate.

20 As seen here, several drugs known to
21 decrease the contraceptive efficacy of norgestrel
22 are used to treat conditions that commonly occur in

1 the population likely to use this product,
2 including medications to treat seizure disorder,
3 anxiety or muscle spasms, HIV, or depression. When
4 concomitant use of an interacting drug cannot be
5 avoided, the prescribing information for norgestrel
6 tablet recommends the use of additional
7 non-hormonal contraception, such as condoms, when
8 initiating and throughout concomitant use of the
9 interacting drug, as well as for 28 days after
10 discontinuation of the interacting drug. However,
11 if use of an interacting drug is expected to be
12 chronic, use of an alternative method of
13 contraception should be considered.

14 As previously mentioned, norgestrel may
15 decrease the contraceptive efficacy of ulipristal
16 acetate emergency contraception when norgestrel use
17 begins within 5 days of ulipristal acetate intake.
18 Therefore, the prescribing information for
19 norgestrel recommends initiating use no sooner than
20 5 days after taking ulipristal acetate for
21 emergency contraception and using additional
22 non-hormonal contraception until the next menstrual

1 period. Because nonprescription use of norgestrel
2 would occur without the assistance of a learned
3 intermediary, opportunities to address additional
4 concerns, such as use in adolescents, potential
5 impact of progestins on bone mineral density, and
6 current use of contraception would be missed.

7 Adolescents are a population of special
8 interest because comprehension of key messages may
9 differ by age group, sexual practices may differ
10 compared to adults, and opportunities may be missed
11 for interactions with and counseling by a
12 healthcare provider. However, we reiterate that
13 prescription norgestrel tablet is approved for use
14 in all females of reproductive potential,
15 regardless of age.

16 Data on the potential impact of progestins,
17 which include norgestrel, on bone mineral density
18 are most readily available for depo
19 medroxyprogesterone acetate injection, which was
20 initially approved for prevention of pregnancy in
21 the United States in 1992. The concern arises from
22 chronic unopposed progestin use, which induces a

1 hypoestrogenic state and may result in decreased
2 bone mineral density in users of any age. The
3 magnitude of this hypoestrogenic effect likely
4 depends on progestin structure, dose, and route of
5 administration.

6 The potential for greatest impact lies in
7 long-term progestin use in individuals who have not
8 yet attained peak bone mass, namely adolescents.
9 Recovery of bone mineral density after
10 discontinuation may also depend on the duration of
11 exposure and the potency of the specific progestin;
12 however, the potential impact of chronic progestin
13 use on fracture risks later in life is unknown,
14 particularly in adolescents.

15 An additional consideration involves the
16 current use of hormonal contraception, or
17 intrauterine system, in individuals desiring to
18 switch to norgestrel tablet. To avoid unintended
19 pregnancy, the prescribing information recommends
20 initiation of norgestrel tablet use the day after
21 discontinuing use of the current method.
22 Norgestrel tablet can be initiated on any day of

1 the week, and additional non-hormonal contraception
2 should be used for the next 48 hours.

3 In addition, there are unique considerations
4 for switching to norgestrel after removal of an
5 IUS. Concomitant use with other hormonal
6 contraceptives, or IUS, is unnecessary. This last
7 statement has been translated to a do-not-use
8 warning in the proposed nonprescription labeling
9 for norgestrel tablet.

10 The considerations I just discussed have
11 important implications for translating effective
12 and safe use of norgestrel tablet to the
13 nonprescription setting. To ensure effectiveness
14 of norgestrel tablet, consumers must be able to
15 understand and adhere to directions for use without
16 the assistance of a learned intermediary, including
17 taking one tablet daily at the same time each day,
18 knowing what to do if a tablet is delayed or
19 missed, or if vomiting or diarrhea occurs within
20 4 hours of taking the tablet, and knowing when to
21 use additional non-hormonal contraception.

22 To ensure safe use of norgestrel tablet in a

1 nonprescription setting, consumers with a history
2 of breast cancer or other progestin-sensitive
3 cancer must be able to deselect from norgestrel
4 use, meaning they must be able to identify that
5 they're not eligible to use norgestrel tablet
6 without the assistance of a learned intermediary.

7 Consumers with abnormal vaginal bleeding
8 must be able to consult a healthcare provider
9 before and during norgestrel use. Consumers who
10 experience bleeding pattern alterations during
11 norgestrel use must be able to recognize the
12 difference between bleeding that requires
13 healthcare provider evaluation and bleeding that
14 may be an adverse effect of norgestrel use.

15 Consumers desiring to use norgestrel, who
16 are also using a drug that may interact with
17 norgestrel, must be able to recognize the need to
18 ask a doctor or pharmacist before use and follow
19 instructions for use of backup contraception.
20 Consumers currently using a hormonal method of
21 contraception, or IUD, who desire to switch to
22 norgestrel tablet, must be able to discontinue the

1 current method and follow instructions for
2 switching to another contraceptive method. And
3 lastly, adolescents must demonstrate comprehension
4 of key labeling messages and the ability to follow
5 directions for use.

6 The key questions, then, for use of
7 norgestrel tablet in the nonprescription setting
8 are the following:

9 Will individuals with breast cancer or other
10 progestin-sensitive cancers correctly self-identify
11 as ineligible for norgestrel?

12 Will norgestrel users identify abnormal
13 vaginal bleeding requiring healthcare provider
14 intervention before and during use?

15 Will norgestrel users understand the risks
16 associated with concomitant use of some drugs,
17 particularly ulipristal acetate?

18 Will individuals understand how to switch
19 from a prescription contraceptive to norgestrel and
20 avoid an unintended pregnancy?

21 My colleagues, Barbara Cohen, Dr. Rongmei
22 Zhang, and Dr. Jeena Jacob will be presenting data

1 from the applicant's submission that attempt to
2 answer these questions.

3 In summary, the efficacy and safety of
4 prescription norgestrel tablet has been established
5 since 1973; however, quantifying effectiveness in
6 the nonprescription setting presents challenges.
7 Uncertainty exists regarding adherence to the
8 recommended dosing regimen and the likelihood of
9 unintended pregnancy.

10 Outstanding safety concerns of particular
11 interest include use of nonprescription norgestrel
12 in individuals with a history of breast cancer or
13 other progestin-sensitive cancer, as well as in
14 individuals with an as yet undiagnosed cancer,
15 abnormal vaginal bleeding of undiagnosed etiology,
16 and drug interactions, particularly with ulipristal
17 acetate emergency contraception; and lastly, use in
18 adolescents presents unique concerns.

19 Thank you for your time and attention. I
20 will now turn it over to my colleague, Barbara
21 Cohen, social scientist in the Division of
22 Nonprescription Drugs II.

1 **FDA Presentation - Barbara Cohen**

2 MS. COHEN: Good afternoon, everybody. I'm
3 Barbara Cohen, the social scientist in the Division
4 of Nonprescription Drugs II, and I'm here today to
5 discuss several of the consumer behavior studies
6 that were part of this NDA application. Before I
7 begin, I'd like to note that this presentation, and
8 all the work that it is based upon, was a joint
9 collaboration between me and Dr. Rongmei Zhang, our
10 statistical reviewer, as well as contributions from
11 Rachel Dlugash, statistical analyst.

12 I further want to emphasize that the
13 analyses I'm going to be discussing were based on
14 extensive consultation with our medical officers,
15 Dr. Anandi Kotak and Dr. Jeena Jacob, as the
16 consumer behavior studies ultimately derived from
17 potential clinical concerns about product efficacy
18 and safety in the nonprescription setting.

19 Here's an outline of my presentation today.
20 In the nonprescription environment, there is no
21 healthcare professional acting as a gatekeeper
22 between the consumer and the drug in question;

1 therefore, consumers need to understand and
2 appropriately act on all warnings and directions
3 for use on their own, with just the labeling to
4 guide them.

5 The Drug Facts Label, or DFL, is the main
6 regulatory foundation for conveying all critical
7 information necessary for safe and effective use of
8 a product. The DFL includes these following
9 sections, and here as an example is the proposed
10 Drug Facts Label that the applicant has submitted.
11 You can see that this DFL in particular has a lot
12 of information for a consumer to take in.

13 In addition to the DFL, there are sometimes
14 the Consumer Information Leaflet inserted into the
15 package, which is also considered to be labeling.
16 This leaflet provides supplementary information on
17 how to use the product, as all critical information
18 is supposed to be on the DFL. The principal
19 display panel, which is the outer box displayed at
20 the point of sale, is also considered to be
21 labeling, as well as the inner blister pack, which
22 is inner plastic packaging sometimes used to seal

1 individual tablets. Blister packs often contain
2 critical messages that reinforce what is displayed
3 elsewhere. Here's the principal display panel for
4 norgestrel.

5 I'm now going to provide an overview of the
6 types of consumer behavior studies utilized in
7 nonprescription regulatory development. In
8 general, consumer studies that are conducted for
9 any specific drug development program flow directly
10 from the nature of clinical concerns, if any, about
11 nonprescription use. Sometimes only one type of
12 study needs to be conducted, and other times, some
13 or all need to be.

14 These studies are conducted by the
15 applicant, ideally in consultation with FDA, and in
16 any event are reviewed by FDA at the time of NDA
17 submission. Label comprehension studies are
18 foundational. The goal of these studies is to
19 assess consumer comprehension of important DFL and
20 CIL statements. Typically, these studies recruit
21 all-comers; that is, anyone who is interested in
22 participating in a study without regard to whether

1 they have a particular condition or need for the
2 product because in many cases, anyone can develop a
3 need for a product, or be a caregiver for someone
4 who needs it, or may be assisting someone else who
5 is considering buying the product for themselves.

6 FDA sometimes asks for adolescents to be
7 included in the studies when adolescents are
8 anticipated to be potentially selecting and using a
9 product on their own. Parental consent is obtained
10 prior to adolescent participation.

11 FDA always asks for approximately 30 percent
12 of the study population to be limited literacy
13 consumers. This number is based on an estimated
14 representation in the U.S. population. The
15 literacy assessment itself is based on the
16 administration of the REALM test, which stands for
17 Rapid Estimate of Adult Literacy in Medicine, and
18 there's also a teen version of this test.

19 Following the REALM assessment, the actual label
20 comprehension interview is conducted. Participants
21 read the DFL on their own, and are then asked
22 scenario questions about hypothetical consumers.

1 It is an open-book test. They can refer to the
2 label at any time when they are being asked a
3 question.

4 While these studies can provide important
5 insights about what is and is not well understood,
6 one of the main limitations in interpretation is
7 that understanding does not always translate into
8 behavior. Therefore, label comprehension studies
9 are necessary but not always sufficient when
10 considering approval of products with significant
11 clinical concerns.

12 Next, I will discuss targeted self-selection
13 studies, which really refer to consumer
14 deselection. What I mean by that is they assess
15 whether consumers can apply understanding of what
16 they read on the label; not to a hypothetical
17 person as in label comprehension, but rather to
18 themselves and their own personal medical
19 situation. They are typically implemented when
20 there's a concern about a specific subpopulation
21 using a product that perhaps has a do-not-use
22 warning on the label for that subpopulation because

1 it represents a contraindication for them. We're
2 looking to see if these consumers accurately state
3 that the product is not medically appropriate for
4 them to use personally, another way of saying is
5 that they correctly deselect.

6 In these studies, participants with a
7 medical condition of concern are recruited without
8 them being explicitly told that that's the reason
9 they were recruited. While we would like to see
10 30 percent limited literacy representation in these
11 studies, we recognize that's not always possible to
12 get the 33 or 30 percent given the difficulties of
13 recruiting people with certain medical conditions,
14 but nonetheless, adequate with limited literacy
15 representation is important.

16 One final note about these studies, the
17 selection decision is the answer to the question,
18 is this product appropriate for you to use given
19 your own personal health circumstances? It is not
20 the answer to the question, would you like to buy
21 this product? That is because the decision to
22 purchase involves many other factors not tied to

1 one's personal medical situation, including, but
2 not limited to, an actual need for the product at
3 that point in time. The rationale for all of this
4 is laid out in FDA's industry guidance on
5 self-selection

6 Actual use studies always have a use phase,
7 and sometimes have an upfront self-selection phase
8 as well. The overall goal of these studies is to
9 assess how consumers decide to use, and then use
10 the the product, in a naturalistic use environment.
11 Typically, recruitment is widespread with both
12 print and digital advertising. Exclusion criteria
13 are supposed to be minimal. If there's an upfront
14 selection phase, consumers read the DFL, and then
15 they are asked whether the drug is appropriate for
16 them to use, again, based on their personal health
17 history.

18 The primary objective of these upfront
19 self-selection phases is often correct deselection
20 because FDA wants to assess whether in a more
21 real-world environment, consumers with a do-not-use
22 or ask-a-doctor-before-use condition adhere to the

1 label. However, we're also interested, usually as
2 a secondary endpoint, in correct selection, which
3 generally is defined as among the study population,
4 how many people made an overall correct decision
5 about the appropriateness of the product given
6 their personal medical situation? By that I mean,
7 how many for whom it was medically appropriate to
8 use, as defined by the label, said it was medically
9 appropriate to use, and how many for whom it was
10 not medically appropriate to use stated as such?

11 Now, all participants who say that a product
12 is appropriate for them to use are asked if they
13 would like to buy it; again, the approach is to
14 simulate a naturalistic environment. All
15 participants, whether they decide to buy it or not,
16 then undergo a medical history interview. Informed
17 consent is administered, and females of
18 reproductive age are asked to take a pregnancy
19 test, as pregnancy is usually an exclusion for all
20 clinical trials. Those with absolute
21 contraindications, a do-not-use condition, are
22 excluded from purchasing. Obviously, in a

1 real-world environment, these would-be purchasers
2 would get through and actually buy, and presumably
3 use it. That is one reason we ask for these
4 studies to be conducted, so we can see how many
5 people ultimately had to be excluded from use.

6 At any rate, at that point, purchasers may
7 enter the use phase of the trial, they take the
8 product home, and use it. The goal of the use
9 phase is to simulate a nonprescription use
10 environment to assess whether a drug can be used
11 properly, safely, and effectively in a naturalistic
12 setting, as naturalistic as possible. A use phase
13 may assess adherence, safety, and effectiveness.

14 Finally, an important word about study
15 thresholds is that primary endpoints are based on
16 what is most clinically important. Multiple
17 endpoints can be designed as co-primary endpoints.
18 In label comprehension studies, primary endpoints
19 of key clinical significance are typically set
20 a priori at 90 percent. In self-selection and
21 actual use studies, deselection endpoints are
22 typically established at 90 percent, and selection

1 endpoints at 85 percent. In the use phase of the
2 actual use studies, many times endpoints such as
3 adherence are typically set at 85 percent. All
4 endpoints are assessed at the lower bound of the
5 two-sided exact 95 percent confidence interval.

6 Now, it's important to note that these
7 thresholds are targets. As we've heard already,
8 they're not hard pass/fail stops if they don't meet
9 the endpoints. However, FDA does differentiate
10 between approaching an endpoint versus being much
11 farther away from achieving it, and when that
12 happens, we do try to look at the reasons behind
13 not achieving endpoints to try to determine if
14 there are ways that these issues can be addressed.
15 Also, although secondary and exploratory endpoints
16 typically do not have thresholds, these are still
17 closely looked at if they represent issues of
18 clinical import.

19 Here's a brief overview of the consumer
20 studies in this population. You could see it on
21 the overall left-hand column. There were two
22 separate pivotal label comprehension studies

1 conducted, one of a Drug Facts Label that's close
2 to a proposed version, and one of an earlier
3 version of the Consumer Information Leaflet. There
4 was a targeted breast cancer selection study and an
5 actual use study known by the acronym, ACCESS, with
6 an upfront self-selection phase. I will be
7 discussing all of these studies in my presentation
8 today, except for the use phase of the actual use
9 study. That will be discussed by my colleagues,
10 Dr. Jeena Jacob and Dr. Rongmei Zhang in their
11 presentations to you today.

12 Now for the label comprehension studies, the
13 pivotal Drug Facts Label, or DFL, comprehension
14 study was conducted among 477 females, ages
15 11 to 50, with no history of breast cancer.
16 Twenty-six percent were of limited literacy. There
17 were 14 primary endpoints with prespecified target
18 thresholds of 90 percent, 19 secondary endpoints,
19 and one other endpoint.

20 FDA examined verbatim responses of each
21 participant to each question to determine whether
22 we agreed when an applicant coded it as correct or

1 acceptable. As a result, four primary endpoints
2 were recalculated, although none changed
3 substantially, i.e., more than 10 percentage
4 points. However, what this in-depth review of the
5 verbatims enabled us to do was to gain insights
6 into area of potential confusion. Today, I will
7 only be discussing those endpoints that are most
8 pertinent to the focus of this meeting, but you can
9 find the results of all the endpoints in the
10 appendix of your backgrounder.

11 Here is comprehension of key DFL statements
12 about adherence, and these endpoints were close to
13 or exceeded the 90 percent threshold. Take one
14 tablet every day. Take one tablet at the same time
15 every day. Do not use together with another
16 hormonal contraceptive. When you finish a pack,
17 start the next one the following day without a
18 break. If you're more than 3 hours late taking
19 your tablet, or if you miss taking it on one or
20 more days, take the tablet immediately as soon as
21 you remember it.

22 However, all DFL statements about the need

1 for backup contraception in certain circumstances
2 scored below the 90 percent threshold: if you have
3 sex in the first 48 hours after starting; if you
4 are late or missed taking a tablet; or if you have
5 vomiting or severe diarrhea. Particularly with
6 regard to that middle statement, the 80 percent
7 lower bound comprehension is a concern because
8 during the course of a busy person's life, there
9 could be many times that for any number of reasons
10 they are, say, more than 3 hours late in taking a
11 tablet or miss it on a day. The applicant states
12 on page 151 of its backgrounder that this should be
13 an infrequent occurrence, but they do not cite any
14 studies to support that assumption.

15 Here are the statements on the DFL about
16 safe use, but with comprehension scores that did
17 not come close to meeting the 90 percent threshold.
18 Do not use if you have, or ever had, breast cancer.
19 This achieved a lower bound of only 80 percent.
20 Here, an examination of the verbatims showed that
21 there was confusion with the other DFL statement
22 about asking a doctor before use with any cancer.

1 And a further concern in analyzing these results by
2 age, we note that among adults, who are, of course,
3 the population at most risk for breast cancer,
4 comprehension of this statement was only 75 percent
5 lower bound.

6 Next, ask a doctor before use if you
7 currently have vaginal bleeding between your
8 periods and have not already talked to a doctor.
9 Comprehension there was 83 percent lower bound.
10 Here, the verbatims revealed confusion with the
11 other statements on the DFL about vaginal bleeding.

12 Here are examples, and you can see an
13 illustration of the cancer confusion. The top
14 arrow is do not use if you had or ever had breast
15 cancer, and the bottom arrow is ask a doctor before
16 use if you have or ever had any cancer. Likewise,
17 with vaginal bleeding, this arrow here on the left,
18 ask a doctor before use if you currently have
19 vaginal bleeding and have not already talked to a
20 doctor versus the two ones on the right that have
21 vaginal bleeding due to use.

22 Finally, do not use as an emergency

1 contraceptive. This product does not prevent
2 pregnancy when used after unprotected sex. This
3 scored at only a 71 percent lower bound. Here
4 there was confusion among other actions to be taken
5 after missing a tablet.

6 I'm going to speak verbally about a slide
7 that I cannot seem to locate in here right now.
8 Oh, it's the ulipristal acetate on the bottom.
9 Dr. Kotak also discussed a concern about drug
10 interactions. Specifically ask a doctor or
11 pharmacist if you have used an emergency
12 contraceptive in the past 5 days. This was a
13 secondary endpoint but an important one because
14 drug interactions can negatively impact the
15 effectiveness of either or both products if taken
16 together. If you look at the lower bound, this was
17 at 78 percent comprehension.

18 Here are adolescents, the breakouts by age
19 group, where there are substantial differences
20 between younger adolescents aged 11 to 14 as
21 compared with older adolescents and adults.
22 Comprehension of when to use barrier contraception

1 and the need to start the next pack the following
2 day without a break was lower in this population,
3 and the difference between norgestrel and emergency
4 contraception was also poorly understood among this
5 age group. As was, ask a doctor or pharmacist
6 before use if ulipristal acetate emergency
7 contraceptive has been used in the past 5 days.

8 With regard to limited literacy
9 comprehension, it's not unusual to have a 10-point
10 difference between normal and limited literacy, but
11 larger differences can point to significant issues.
12 Here, you can see that there were very large
13 differences in understanding of do not use an
14 emergency contraceptive. There were also large
15 differences with regard to the need for barrier
16 contraception if a tablet is later missed, as well
17 as asking a doctor or pharmacist before use if you
18 have taken ulipristal acetate in the past 5 days.

19 Now I will very briefly touch on the
20 Consumer Information Leaflet, or CIL, comprehension
21 study. This was conducted in 2017 among
22 551 females and males, ages 11+, 25 percent of

1 limited literacy. Now it's important to note that
2 this CIL evaluated six years ago is not the
3 currently proposed CIL, but it was the CIL utilized
4 in the ACCESS study. The applicant did not
5 establish any primary endpoints, contending that
6 all information on the CIL was supplementary, but
7 FDA does not agree.

8 Now, the reason we don't agree with the
9 applicant that all information on the CIL was
10 supplementary was that there are two important
11 statements there that are not even on the DFL.
12 Thus, there is not the opportunity to reinforce
13 those on the DFL if they are not understood here.
14 The first is, if you are switching from another
15 birth control pill, vaginal ring, or patch, start
16 taking Opill the day after you stop the other
17 method. The DFL refers to the CIL for the
18 information, but it does not provide this
19 information directly. That is left to the CIL.
20 The lower bound was 78 percent.

21 The verbatims revealed confusion with the
22 other directions on the CIL, with participants

1 citing other transition periods mentioned of 2 days
2 or 5 days. The second was, what if I have taken an
3 emergency contraceptive before starting Opill? Use
4 a condom or barrier method every time you have sex
5 until your next period. That comprehension was
6 77 percent. For adolescents, there were no
7 substantial differences in comprehension, with one
8 notable exception; comprehension about the need for
9 a barrier method after taking an emergency
10 contraceptive, and with regard to the limited
11 literacy subgroup, there was a lot less
12 understanding of both key CIL-only statements.

13 Finally, the discussion of the design and
14 interpretation limitations; again, no thresholds
15 were prespecified. Secondly, placement and wording
16 of some statements in the tested version were
17 revived in the currently proposed CIL, as were the
18 design and illustration. All of these changes
19 could impact comprehension; therefore, the
20 comprehension scores may have limited utility in
21 assessing comprehension at this point.

22 Now, I'll discuss the targeted breast cancer

1 self-selection study. The objective of the study
2 was to evaluate the adequacy of the DFL in
3 facilitating correct deselection by females with
4 breast cancer, and there was a 90 percent threshold
5 for this endpoint. The study was conducted among
6 206 females ages 18 to 50 with a current or past
7 history of breast cancer; but of note, only
8 5 percent were of limited literacy. As with the
9 label comprehension study, because it was conducted
10 simultaneously with that study, it was based on a
11 slightly different version of the currently
12 proposed label, but this was not different
13 regarding the breast cancer statement.

14 Importantly, the participants were not
15 informed as to the reason they were recruited, and
16 again, the critical self-selection question was,
17 given what you have read on the label and your own
18 health history, is this product okay or not okay
19 for you personally to use?

20 The results show that the threshold was
21 achieved but, again, this was in an almost total
22 normal literacy population. The applicant reported

1 correct deselection was 94 percent, but I want to
2 point out this still does involve 6 participants
3 who incorrectly stated it was okay to use. These
4 results also include the seventh who said it was
5 ok, who the applicant then subsequently agreed it
6 was ok, but FDA did not agree on the seventh
7 participant. And we also classified four
8 additional participants as incorrect selectors
9 because they stated that they would need to ask a
10 doctor rather than automatically articulating that
11 it was an absolute contraindication.

12 Part of the reason we're being very
13 conservative about this coding is because if
14 someone states they would ask the doctor, it's
15 unclear whether they would do so before starting
16 use of a product, particularly if this doctor is
17 not easily accessible to them. The FDA reported
18 the correct deselection endpoint was 91 percent,
19 which still exceeded the threshold. We conducted
20 some further sensitivity analyses, and the correct
21 deselection still approximated the threshold at
22 88 percent.

1 In summary, although many females with
2 current or previous breast cancer may correctly
3 deselect from taking norgestrel, some will likely
4 consider it appropriate to use. But even meeting a
5 90 percent threshold does not mean that
6 deselection, again, would be perfect across the
7 population since up to 10 percent could still not
8 properly deselect.

9 Now, the full extent of this issue and the
10 resulting implications are not clear. Since only
11 5 percent of the study population was of limited
12 literacy, it is unclear whether we can generalize
13 these study results to a real-world setting of
14 30 percent limited literacy, where potentially
15 correct deselection could be substantially below
16 this 90 percent threshold.

17 The last study I will discuss today is the
18 self-selection phase of the ACCESS study. The
19 primary objective of this study, per FDA, was to
20 evaluate the adequacy of the DFL in facilitating
21 correct deselection by females with medical
22 conditions of clinical concern, such as breast

1 cancer and abnormal vaginal bleeding; that is, did
2 those females correctly decide it was not
3 appropriate to use in accordance with the label?
4 The applicant declined to make this the primary
5 endpoint.

6 The secondary objective, per FDA, was to
7 evaluate the adequacy of the DFL in facilitating
8 overall correct selection among the population;
9 again, that is to say for those whom it was
10 medically appropriate to use, how many said it was
11 medically appropriate, and for those whom it was
12 not medically appropriate, how many said that? The
13 applicant made this the primary endpoint.

14 The study was conducted among
15 772 participants. Limited literacy was only
16 13 percent representation in this study. The
17 ACCESS study utilized a prior version of the DFL,
18 one that said do not use for any cancer. I'll say
19 more about this in a minute. Here is the DFL that
20 was used. It was do not use if you have ever had
21 any cancer. Here are the self-selection questions
22 that were asked, and here are the purchase

1 questions, which were asked if the self-selection
2 question was yes.

3 Now, much of the difference between our
4 results and the applicant's is due to the fact that
5 367 of the 772 participants stated that Opill was
6 appropriate with their personal health history, but
7 they did not want to purchase it mostly because
8 they were already using a birth control or they
9 didn't have need for a birth control. The
10 applicant decided that for each one of these
11 participants, even though each said it was
12 appropriate for them to use with their personal
13 health history, that each of these people actually
14 meant it wasn't appropriate because they ultimately
15 didn't purchase it.

16 The applicant used the purchase decision to
17 overrule the selection decision, and they therefore
18 classified each as saying it was not appropriate to
19 use or non-selectors. In contrast, our position in
20 review of this application is consistent with our
21 industry guidance, which states that lack of
22 purchase does not alter the self-selection

1 decision. If people don't have a current need for
2 a product at the time of the enrollment interview,
3 they didn't purchase it, but that doesn't mean they
4 could not evaluate at all their medical
5 appropriateness to use that product.

6 The applicant reported correct deselection
7 was 75 percent lower bound. Now, I want to point
8 out this was already substantially below the
9 90 percent deselection threshold. The FDA-analyzed
10 correct deselection was 18 percent, and for correct
11 selection, the applicant reported correct selection
12 was 99 percent lower bound and the FDA correct
13 selection was 83 percent lower bound, but I want to
14 note that this 83 percent does approximate the
15 85 percent typical correct selection threshold.

16 I've already talked about the first major
17 reason for this difference in results. A second
18 reason was that the applicant conducted a post hoc
19 mitigation of some participants with cancer,
20 unexplained vaginal bleeding, and liver disease,
21 and other conditions, and determined that in some
22 of these instances, it was medically acceptable for

1 them to use. FDA medical reviewers did not concur
2 with many of these mitigations regarding cancer,
3 unexplained vaginal bleeding, and liver disease.

4 Finally, the overall study design was
5 problematic. First, there was a lack of a study
6 pathway for participants to actually follow the DFL
7 and ask their doctor first, when relevant, and then
8 return to the study. Secondly, that lack of the
9 pathway could have been at least somewhat
10 ameliorated by precisely determining when exactly
11 participants talk to a doctor if they stated they
12 had at any point in the study, but there was also
13 no data collected to elicit whether they consulted
14 a doctor after purchase but before use.

15 Now I'll discuss the subgroups with clinical
16 issues of concern; first, participants with cancer.
17 As noted previously, this study was based on an
18 earlier version of the DFL, one that said do not
19 use with any cancer. Out of the 14 participants
20 with cancer, eleven stated that it was appropriate
21 for them to use.

22 Now, I want to make clear the point of this

1 slide is not to say that we say that all eleven
2 were inappropriate to use because that is not
3 actually what the current label says today. The
4 point is that all eleven ignored the warning of "do
5 not use" that was on the label at that time, that
6 pertained to their current situation. That is our
7 concern; that even though the current warning of do
8 not use pertains to breast cancer only, that in
9 like fashion, females with breast cancer would
10 ignore the current warning.

11 As you'll recall, we saw that that did
12 happen to some degree in the targeted breast cancer
13 study. In this study, specifically of the eleven,
14 two did have breast cancer. One tried to purchase
15 and had to be excluded from use. The other said
16 she would talk to her pharmacist rather than
17 automatically deselecting, according to the "do not
18 use" on the label. Another participant, someone
19 with metastatic melanoma, also tried to purchase
20 and had to be excluded. Again, in an in-market
21 situation, these people would have gone ahead and
22 purchased the product. Here's the breakdown of the

1 participants with cancer, and you can refer to this
2 in the slide deck if you'd like to look at it more
3 carefully.

4 Now I'll discuss participants with
5 unexplained vaginal bleeding. The ACCESS DFL
6 stated to ask a doctor before use if you have
7 unexplained vaginal bleeding between periods. The
8 current DFL adds, and if you've already talked to a
9 doctor. During the self-selection interview,
10 25 participants stated that they had unexplained
11 vaginal bleeding and that they had not spoken to a
12 doctor about it. Of those, 17 out of 25 failed to
13 correctly deselect; in other words, they said it
14 was appropriate for them to use it. Nine purchased
15 the product.

16 Now, this was a relative contraindication
17 and not an absolute one, and therefore they were
18 not excluded and continued into the ACCESS study.
19 Because of the study design issues that I noted
20 previously regarding lack of data around asking a
21 doctor before used, and because the nature of the
22 bleeding issue was sparse in many instances from

1 the medical history interview, our medical
2 reviewers felt they needed to assess all as being
3 inappropriate to use.

4 Regarding adolescents, of the
5 363 adolescents in the self-selection population,
6 one, age 15, had thyroid cancer and correctly
7 deselected according to the label. Five had
8 unexplained vaginal bleeding, but only one of the
9 five stated that it was inappropriate medically for
10 her to use. Furthermore, the study was not
11 designed to systematically capture data on
12 off-label usage. Of a total of 50 study
13 participants who stated at some point that they
14 intended to or were using the product off label, 27
15 were adolescents.

16 Finally, with regard to limited literacy,
17 3 participants with cancer were of limited
18 literacy. Only one correctly adhered to the DNU on
19 the label and correctly deselected, and one of the
20 incorrect selectors with limited literacy had
21 breast cancer. Four participants with unexplained
22 vaginal bleeding were of limited literacy, and only

1 one of the four correctly stated that it was not
2 medically appropriate for her to use the product.

3 In summary, I'll summarize the key
4 takeaways. Regarding breast cancer, the
5 appropriate action is to deselect from norgestrel
6 use. This had mixed results. In the DFL label
7 comprehension, comprehension was 80 percent. The
8 targeted breast cancer study met its threshold but
9 still, at a minimum, 7 out of 206 failed to
10 correctly deselect, and with 5 percent limited
11 literacy representation it is unclear how, if
12 anything, this would be generalizable to the actual
13 population of females who would be interested in
14 potential norgestrel use. In the ACCESS study,
15 both breast cancer participants failed to correctly
16 deselect. One of limited literacy had to be
17 excluded from purchase.

18 Regarding unexplained vaginal bleeding, the
19 label comprehension study, understanding of ask a
20 doctor before use was 83 percent. In the ACCESS
21 study, 17 out of 25 participants with unexplained
22 vaginal bleeding failed to correctly deselect.

1 With regard to drug interactions, comprehension of
2 ask a doctor before use of ulipristal acetate was
3 78 percent, and comprehension of the need for
4 backup contraception with its use was 77 percent.

5 With regard to adolescents, ages 11 to 14
6 demonstrated particularly low comprehension of the
7 need for backup contraception after missing or
8 being late with a dose and with the use of
9 ulipristal acetate, and starting the next pack the
10 day after you finish the last one. Both younger
11 and older adolescents demonstrated low
12 comprehension of do not use as an emergency
13 contraceptive. Four of five adolescents in ACCESS
14 did not correctly deselect with unexplained vaginal
15 bleeding, and there was adolescent off-label intent
16 to use in ACCESS as well.

17 With regard to limited literacy, there was
18 inadequate understanding of do not use as an
19 emergency contraceptive, use a condom or barrier
20 method if late or missing a dose, or after using
21 ulipristal acetate, and of the need to start taking
22 Opill the day after you stop taking another birth

1 control method. Additionally, there were issues
2 with the low representation of the limited literacy
3 population.

4 In conclusion, there were very mixed results
5 regarding breast cancer deselection and relatively
6 low comprehension and inadequate deselection about
7 the need to ask a doctor before use with
8 unexplained vaginal bleeding. Although overall,
9 deselection is poor, the overall proportion of
10 total study participants who made a correct
11 decision about their medical appropriateness to use
12 Opill approaches the prespecified threshold.

13 Finally, with regard to understanding of the
14 key DFL statements regarding effectiveness, there
15 was high comprehension of many key aspects of use;
16 but particularly for limited literacy in
17 adolescents, low comprehension of the need to use
18 backup contraception when late or missing a dose,
19 or after ulipristal acetate, as well as lack of
20 comprehension of the difference between norgestrel
21 and an emergency contraceptive.

22 Thank you for your time, and I now turn the

1 presentation over to Dr. Jeena Jacob.

2 **FDA Presentation - Jeena Jacob**

3 DR. JACOB: Good afternoon. My name is
4 Jeena Jacob, and I'm a medical officer in the
5 Division of Nonprescription Drugs II. In this
6 presentation, I will be speaking about the design
7 and conduct of the use phase of the ACCESS actual
8 use study. The applicant has included many aspects
9 of the design of the actual use study in their
10 presentation, and therefore, in the interest of
11 time, I will be skipping over certain slides and
12 abbreviating my discussion in this presentation.

13 This slide outlines my presentation.
14 First, I will discuss the actual use studies in the
15 development program. I will then discuss the
16 ACCESS study design followed by the ACCESS results,
17 including the phenomena, improbable dosing.

18 The applicant conducted two actual use
19 studies. The pivotal actual use study was the
20 ACCESS study, which was conducted between
21 September 2019 and August 2021. The OPTION study
22 was planned as a 16-week study; however, it was

1 terminated early due to technical issues with the
2 medication use e-diary, which included the
3 participants not being able to access the e-diary
4 and enter data for a period of time. None of the
5 planned endpoints were analyzed in the study. I
6 have mentioned the OPTION study to be
7 comprehensive, but the remaining presentation will
8 focus only on ACCESS as the pivotal actual use
9 study for norgestrel.

10 The applicant has presented the design of
11 ACCESS, and I will not cover this information in
12 detail. Regarding norgestrel dispensing, note that
13 participants were permitted to purchase up to
14 8 packs over the course of the the study. There
15 may have been several issues with respect to the
16 e-diary design. The data entry was retrospective
17 and vulnerable to recall bias. Not only was the
18 data entry form not visible to participants until
19 the next day, the e-diary also allowed participants
20 to enter data for up to 10 days.

21 The screenshot on this slide displays the
22 screen seen by the participants when they had

1 missed diary entries. If a participant did not
2 open the e-diary and enter data for any of the
3 previous days in the 10-day look-back period, the
4 e-diary prompted a participant to begin entering
5 data at the oldest available day, and complete the
6 diary for each day until they reach the entry for
7 that day. The e-diary also asked participants if
8 they took an additional tablet up to 4 times each
9 day, which may have prompted participants to enter
10 data in a manner that may have increased likelihood
11 of overreporting of use.

12 There were a few study design issues that
13 are notable. The compensation structure for the
14 study was designed in such a way that participants
15 were paid for each day they completed their e-diary
16 regardless of whether they reported taking the
17 study drug or not. It is possible that this may
18 have influenced the entering of information, even
19 if the information recorded was not accurate.

20 Participants less than 18 years old were not
21 asked to report sexual activity, and it was
22 therefore unclear how many of the adolescent

1 participants were at risk for pregnancy, as well as
2 how many performed mitigating behaviors such as
3 abstinence or use of barrier contraception when
4 engaging in sexual activity when either initiating
5 use of the study drug or in the setting of a missed
6 or late tablet. Also, the timing and precise
7 content of discussion between study participants
8 and healthcare providers was not captured for the
9 purposes of analysis of all of the secondary
10 endpoints. This limited the interpretation of
11 secondary endpoints and whether there was adherence
12 to critical safety messages in the proposed DFL.

13 This table outlines the primary endpoints of
14 the ACCESS study. There were four primary
15 endpoints in the ACCESS study. Primary endpoint A
16 was a self-selection endpoint discussed by my
17 colleague, Barbara Cohen, in her presentation.
18 Primary endpoints B, C, and D are adherence
19 endpoints. Because efficacy of this product is
20 affected by correct use, adherence endpoints are
21 critical to assessing effective use in the
22 nonprescription setting, and FDA has previously

1 requested a 90 percent threshold for all primary
2 endpoints. The analysis of these endpoints will be
3 discussed by my colleague, Rongmei Zhang,
4 statistical reviewer, in her presentation. There
5 are also 16 secondary endpoints which will be
6 discussed separately later.

7 Regarding study participant disposition, a
8 few items are of note. Twenty-one percent of
9 participants withdrew from the study and 25 percent
10 were lost to follow-up. Only 46 percent of
11 participants had a known result for end-of-study
12 pregnancy test.

13 This slide highlights the demographics of
14 the user population. I would like to note that
15 6 percent of the participants in the user
16 population were reported as being in the
17 11-to-14 age group; however, there were only
18 3 participants who were 12 years old and none who
19 were 11 years old.

20 On this slide, I would like to highlight the
21 14 percent of participants in the user population
22 who had limited literacy. This is a substantial

1 underrepresentation of limited literacy when
2 compared to the U.S. population, and it is possible
3 that this study may overestimate the results of
4 appropriate use when compared to the general
5 consumer population.

6 In the next few slides, I will be discussing
7 the phenomena of improbable dosing, which has had a
8 major impact on the ACCESS study. As discussed by
9 the applicant this morning, improbable dosing is
10 defined as when the total tablets reported taken by
11 a participant exceeded the total number of tablets
12 that were reported as dispensed to that
13 participant.

14 Although the applicant did not note this in
15 the study report at the time of the supplementary
16 NDA submission, upon review of the submitted data,
17 FDA queried the applicant whether there were
18 participants who reported more tablets taken than
19 the total number of tablets dispensed. The
20 applicant confirmed that there were participants
21 with reported tablets taken that was greater than
22 the number of tablets dispensed.

1 The applicant later reported that there were
2 261 participants, which comprised 30 percent of the
3 user population who reported taking more tablets
4 than dispensed, and refer to this phenomena as
5 improbable dosing. The applicant then
6 retrospectively conducted and submitted the
7 results, a qualitative follow-up study, that
8 consists of interviews with participants who
9 reported improbable dosing.

10 At FDA's request, the applicant also
11 submitted a root cause analysis of reasons why
12 improbable dosing occurred. I will not be
13 reviewing the design of the improbable dosing
14 follow-up study in the interest of time, but note
15 that only 29 percent of participants with
16 improbable dosing participated in the study.

17 Almost half of the participants in this
18 study reported inadvertently reporting excess
19 tablets. About one-third reported that they had
20 access to additional birth control of which
21 78 percent reported access to receiving more
22 adjustable packs from study site. There were

1 3 participants who reported receiving more
2 norgestrel packs from another study participant,
3 and 2 participants said that they reported use of
4 birth control other than norgestrel in the e-diary.

5 There were a number of limitations for the
6 interpretation of the results of the study,
7 including recall bias, that the length of time that
8 elapsed after completion of ACCESS in the study
9 ranged from 1 to 3 years. This was also a limited
10 sample of the improbable dosing population that was
11 not representative of the entire improbable dosing
12 cohort. This has the potential to introduce bias
13 into the study and affect the study results. There
14 was no standardized format of questions, which
15 would lead to vastly different questions being
16 asked to different participants.

17 Overall, the number of limitations in the
18 design of the study presented a barrier to
19 meaningful interpretation of the presented results,
20 and FDA concluded that the study did not inform
21 clear reason for improbable dosing. Because the
22 study did not address a root cause of the issue of

1 improbable dosing occurring in the actual use
2 study, FDA requested the applicant to conduct a
3 comprehensive root cause analysis to determine
4 where errors occurred.

5 This table displays root causes identified
6 in the applicant's submission. First, the
7 applicant's submission identified the absence of a
8 study design element for prevention of participant
9 improbable dosing, as well as the study design not
10 having a focus on identifying reported improbable
11 dosing by study participants. The root cause
12 analysis noted that training for sites and nurse
13 interviewers did not focus on identifying
14 improbable dosing, and study plans do not have
15 steps to identify improbable dosing.

16 The applicant's root cause analysis also
17 noted that there were issues related to the setup
18 of e-diary, including not alerting participants who
19 were trying to enter doses they had not been
20 supplied with, and that the participants were able
21 to enter data until the e-diary was deactivated.
22 Participants received reminders to complete the

1 e-diary until the e-diary was deactivated, which
2 may have occurred after the participant had
3 returned study drug or no longer had study drug
4 available.

5 The applicant conducted a demographic
6 analysis of participants in the improbable dosing
7 group and found that participants who had limited
8 literacy were African American, had an education
9 level of high school or less, and had an income of
10 less than 25,000 dollars were disproportionately
11 represented in the improbable dosing group.

12 Demographics such as age and a history of hormonal
13 birth control use were not different between the
14 probable dosing and improbable dosing groups.

15 The FDA Office of Scientific Investigations
16 completed an inspection of select investigational
17 sites. They concluded that the supplementary NDA
18 data for the study medication tablets dispensed to
19 the participants, and reported by the participants
20 as taken, were verifiable against the data
21 documented on source records and case report forms.
22 The root cause of improbable dosing was not

1 discovered.

2 Although the applicant's submission provided
3 risk mitigation measures that might have prevented
4 the phenomena of improbable dosing, a definitive
5 root cause was not identified. The applicant's
6 root cause analysis stated that participants may
7 have overreported due to financial incentives,
8 which is speculative, and given the available data,
9 it is still unclear whether participants in the
10 improbable dosing population incorrectly used the
11 study drug, whether the e-diary incorrectly
12 captured use of the study drug, or there were other
13 reasons.

14 The magnitude of improbable dosing in ACCESS
15 is a limitation in the assessment of adherence
16 endpoints and raises concerns regarding whether the
17 data in the actual use study can be relied upon, as
18 other participants who are not part of the
19 improbable dosing group may have incorrectly used,
20 or incorrectly reported use, who are not identified
21 with improper use.

22 The magnitude of improbable dosing in ACCESS

1 is a limitation in the assessment of adherence
2 endpoints and raises concerns regarding whether the
3 data in the actual use study can be relied upon.
4 The FDA analyses of adherence endpoints included
5 analyses that excluded data of participants with
6 improbable dosing, as well as analyses that
7 classified participants with improbable dosing
8 having reported incorrect use.

9 Thank you. I will now pass it to my
10 colleague, Rongmei Zhang, who will be speaking
11 about the statistical analysis of the primary
12 endpoints in ACCESS.

13 **FDA Application - Rongmei Zhang**

14 DR. ZHANG: Good afternoon. I'm Rongmei
15 Zhang, mathematical statistician in the Division of
16 Biometrics VII in the Office of Biostatistics. I'm
17 here today to discuss the use and adherence
18 endpoints in the ACCESS study. I would like to
19 first acknowledge my colleague, Ms. Rachel Dlugash,
20 the statistical analyst in the Office of
21 Biostatistics, for her assistance in the
22 statistical analysis.

1 My presentation will start with
2 participants' disposition, and then discuss the
3 basis of adherence analysis, which is the study
4 days. The focus of my presentation is the
5 adherence primary endpoint. This includes taking
6 one tablet every day and taking one tablet at the
7 same time every day. I will also present FDA's
8 sensitivity analysis about improbable dosing and
9 summarize our findings in the end.

10 As Dr. Jacob discussed in her presentation,
11 there are a total of 883 participants in the user
12 population. Among them, 53 percent completed the
13 study and the end of the study interview;
14 26 percent were loss to follow-up; and 21 percent
15 withdrew from the study.

16 In the ACCESS study, participants used
17 e-diary to report the date and the time of each
18 dose taken. This figure illustrates a
19 participant's self-reported use. Each green solid
20 square represents a day reported taking at least
21 one tablet of norgestrel. Each red-shaded square
22 represents a day reported not taking norgestrel,

1 and each yellow empty square represents a day with
2 no data entry in e-diary. The days considered in
3 the analysis are active use study days, or AUSD,
4 defined as the study days between a participant's
5 first reported use and their last reported use. In
6 the example here, this participant reported
7 35 AUSDs, including 26 days taking norgestrel,
8 3 days not taken norgestrel, and 6 days with no
9 data entry in her e-diary.

10 Next, I will discuss primary endpoints B and
11 C, which evaluated taking one tablet every day.
12 The dosing day analysis of primary endpoint B adds
13 up the study days across different participants.
14 In this example, 3 participants had a total of
15 321 days taking norgestrel, 3 days not taking
16 norgestrel, and 46 days without data entry. In the
17 ACCESS study, the per protocol analysis was an
18 analysis excluding the days without data entry in
19 e-diary, and in contrast, the worst-case analysis
20 included those days and imputed them as not taking
21 norgestrel. In this example, correct daily
22 adherence in per protocol analysis is 99 percent,

1 and in the worst-case analysis, where the days
2 without data entry were imputed as incorrect, the
3 correct daily adherence is 87 percent.

4 In the ACCESS study, in total, there are
5 over 90,000 AUSDs for the 883 participants in the
6 user population. This includes over 80,000 days
7 reported taken at least one dose of norgestrel,
8 over 6,000 days reported not taking norgestrel, and
9 over 6,000 days without data entry in the e-diary.
10 In contrast to dosing day analysis, the
11 participant-level analysis, or primary endpoint C,
12 analyzes the daily adherence within participants
13 first, and then calculates the proportion of
14 participants who took norgestrel at least
15 85 percent of the days.

16 In this example, in the per protocol
17 analysis, all 3 participants took norgestrel at
18 least 85 percent of the days, which result in a
19 total of 100 days correct adherence. However, in
20 the worst-case analysis, days without data entry
21 were imputed as not taking norgestrel, and only one
22 participant took norgestrel at least 85 percent of

1 the days, and this results in a total of 33 percent
2 correct adherence.

3 In the ACCESS study, if we look at the
4 participant level, the active use study days per
5 participant varied from 1 to 195 days, with an
6 average of 109 days. This slide summarizes the
7 definition and analysis for primary endpoints B
8 and C. For each endpoint, we will present two
9 analyses. As shown in the previous examples, per
10 protocol analysis excluded days without data entry
11 in e-diary, and the worst-case imputed no data
12 entry days as not taking norgestrel. Both
13 endpoints have a prespecified threshold of
14 85 percent lower bound, meaning that the lower
15 bound of the two-sided 95 percent confidence
16 interval needs to be at least 85 percent.

17 Results show that for the daily adherence,
18 the dosing day analysis for endpoint B met its
19 threshold, but the participant level analysis,
20 endpoint C, did not. The lower bound for the
21 correct adherence for endpoint C is 82 percent and
22 68 percent for the per protocol and worst-case

1 analysis, respectively.

2 In the next few slides, I will discuss
3 taking one tablet at the same time every day, which
4 is essential for the effectiveness of norgestrel.
5 Note that in the same time evaluation, each dose is
6 compared to its previous dose, and the same time
7 criterion is met if the dose was taken no later
8 than 3 hours after or 3 hours before the time for
9 the previous dose taken.

10 Before presenting the result, I want to
11 emphasize the different definitions of days
12 included for the time of dose in the applicant's
13 and FDA's analysis. As shown in this table, FDA
14 and the applicant used the same approach to analyze
15 days taking norgestrel and days with no data entry
16 in the e-diary. The difference between FDA's and
17 the applicant's analysis is that the applicant
18 excluded the days not taking norgestrel from their
19 analysis, but FDA included them and considered them
20 as incorrect time of dose.

21 This table provides the applicant's
22 definition of primary endpoint D, which is to

1 evaluate taking norgestrel at the same time every
2 day. The applicant did not conduct a
3 participant-level analysis for this measure.
4 Again, the per protocol analysis excluded the days
5 with no data entry in e-diary, and worst-case
6 analysis imputed them as incorrect time of those.

7 As explained in my last slide, the days
8 included for time of dose was defined differently
9 by FDA and the applicant; therefore, we call the
10 FDA primary endpoints D1 and D2. D1 is a dosing
11 day analysis and D2 is a participant-level
12 analysis, where a participant was considered
13 correct adherence if she took norgestrel at the
14 same time at least 85 percent of the days
15 evaluable.

16 Results show that all dosing day analysis
17 endpoints D and D1 met the threshold of 85 percent
18 lower bound, but the FDA participant-level
19 analysis, endpoint D2, did not. The lower bound of
20 the correct adherence for D2 is 71 percent and
21 59 percent for per protocol and worst-case
22 analysis, respectively.

1 In the next few slides, I will be discussing
2 improbable dosing and FDA's sensitivity analysis.
3 As Dr. Jacob discussed in her presentation, about
4 one-third of the user population reported taking
5 more doses than the doses dispensed or the
6 improbable dosing problem. Because of the actual
7 use behavior of these participants, with the
8 improbable dosing unclear, we conducted two
9 sensitivity analyses. One is to exclude
10 participants within improbable dosing, and the
11 other is to classify them as incorrect in
12 participant-level analysis, and to classify their
13 study days as incorrect in dosing day analysis.

14 As you can see here, for primary endpoints B
15 and C, in the analysis excluding participants with
16 improbable dosing, the correct adherence was about
17 1 to 2 percent lower than the analysis using all of
18 the participants. As expected, classifying
19 participants with improbable dosing as incorrect
20 substantially reduces correct adherence. A similar
21 pattern was found in the evaluation for the time of
22 dose. Excluding participants with improbable

1 dosing reduces the correct adherence about 2 to
2 3 percent; however, classifying them as incorrect
3 substantially reduces the correct adherence about
4 20 to 30 percent.

5 In summary, under different assumptions, the
6 correct response for daily adherence varied from
7 46 to 92 percent lower bound, and the correct
8 response for daily same time adherence varied from
9 39 percent to 96 percent lower bound.

10 In conclusion, uncertainties about accuracy
11 for e-diary reporting calls into question the
12 reliability of the ACCESS user phase to assess
13 adherence to instructions in the Drug Facts Label
14 necessary for pregnancy prevention. More
15 specifically, it is unclear if improbable dosing is
16 incorrectly used, or incorrect e-diary entry, or
17 other reasons. Also, the large proportion of the
18 participants with improbable dosing raise concerns
19 about the accuracy of the e-diary reporting among
20 the participants who did not report taking more
21 tablets than dispensed.

22 Thank you for your time. I will now turn it

1 over to my colleague, Dr. Jacob.

2 **FDA Presentation - Jeena Jacob**

3 DR. JACOB: Thank you.

4 This is Jeena Jacob, medical officer in the
5 Division of Nonprescription Drugs II. In this
6 presentation, I will be speaking about the
7 secondary endpoints in the ACCESS use phase, as
8 well as the safety findings from uncontrolled and
9 postmarketing data. Again, in the interest of
10 time, I will be skipping over certain slides and
11 abbreviating the discussion of other slides.

12 This slide provides an outline of my
13 presentation. First, I will discuss the secondary
14 endpoints in the ACCESS study. I will then discuss
15 the safety data in ACCESS and the postmarket data.
16 I will then end with conclusions about the ACCESS
17 actual use study.

18 The first section of this presentation will
19 focus on the ACCESS secondary endpoints. As we
20 have discussed earlier, the magnitude of improbable
21 dosing in the study raises questions about whether
22 the data in the actual use study can be relied

1 upon, including the analyses of some of the
2 secondary endpoints.

3 This table displays the classification of
4 the secondary endpoints in ACCESS. Secondary
5 endpoint A was discussed in the presentation of the
6 self-selection component of the ACCESS study. I'm
7 only going to highlight a few of the secondary
8 endpoints in the next few slides. The results of
9 the secondary endpoint analysis are highlighted in
10 the briefing document.

11 This slide displays adherence to the message
12 of do not use norgestrel together with another form
13 of hormone-containing birth control product. FDA
14 concurs with the applicant's result of
15 approximately 99 percent. Of note, of the
16 11 participants who reported concomitant use of
17 another hormonal contraceptive, five were
18 adolescents.

19 Secondary endpoint I also had high adherence
20 to the corresponding DFL message. Secondary
21 endpoint I tests adherence to the message on the
22 DFL that instructs consumers to stop use and ask a

1 doctor if you become pregnant to minimize the risk
2 in the delay of a pregnancy diagnosis. The
3 denominator of this analysis includes all
4 pregnancies that were classified as having a date
5 of conception pretreatment or on treatment.

6 Although participants may have had a
7 negative pregnancy test prior to entering the use
8 phase of the study, it is possible that they may
9 have become pregnant pretreatment and had a
10 negative urine pregnancy test at enrollment. The
11 FDA analysis differs from that of the applicant
12 because the applicant classified 6 participants as
13 becoming pregnant pretreatment or on treatment,
14 which is why the denominator of the applicant
15 analysis is 6. The FDA review team classified
16 10 participants as becoming pregnant pretreatment
17 or on treatment, which is why the FDA analysis has
18 a denominator of 10.

19 The FDA analysis resulted in 80 percent of
20 participants who became pregnant pretreatment or on
21 treatment as performing the correct follow-up
22 action. The FDA's analysis differed from the

1 applicant's in several instances because the
2 applicant only included participants who reported
3 the pertinent symptoms and completed the end of
4 study interview in the denominator of the analysis,
5 and FDA's analysis included all participants who
6 experienced the symptom or event during the study
7 in the denominator.

8 The numerator differs in the FDA analysis
9 and the applicant analysis because the FDA analysis
10 only classifies correct, participants who spoke to
11 healthcare provider about the specified symptom,
12 while the applicant analysis classifies as correct
13 all participants who spoke to a healthcare provider
14 for any reason, at any time, and not just about the
15 particular symptom being evaluated.

16 For example, in this slide, secondary
17 endpoint L tests the DFL message, which instructs
18 consumers to talk to a doctor and continue taking
19 every day if they experience periods that last more
20 than 8 days or are usually heavy. Long and heavy
21 periods can be a potential safety issue, as this
22 can be a sign of a medical condition of undiagnosed

1 etiology, such as malignancy that warrants medical
2 evaluation. The applicant's analysis only included
3 participants who reported these symptoms and
4 completed the end-of-study interview in the
5 denominator of the analysis, while the FDA analysis
6 includes all participants reported these symptoms
7 during the study.

8 The numerator in the applicant's analysis
9 includes as correct all participants who either
10 stopped the study drug or spoke to a healthcare
11 provider for any reason at any time during the
12 study. Notably, two of the participants who were
13 assessed as correct by the applicant had an
14 interaction with a healthcare provider that
15 occurred before the report of prolonged or heavy
16 periods. The numerator in the FDA analysis only
17 classifies participants who spoke to a healthcare
18 provider about the specified symptoms as correct,
19 and this yielded a result of 18 percent.

20 This slide also outlines endpoints that
21 demonstrated low adherence to DFL messages.
22 Secondary endpoint J tests adherence to the message

1 to seek medical care for sudden or severe abdominal
2 pain, as this can be a sign of a potentially life-
3 threatening condition such as ectopic pregnancy.
4 The FDA analysis differed from that of the
5 applicant because the applicant's analysis
6 classified all participants who spoke to a
7 healthcare provider for any reason at any time
8 during the study as having completed a correct
9 action, while the FDA analysis only classified
10 participants who spoke to a healthcare provider
11 specifically about abdominal pain as correct.

12 Notably, two of the participants that were
13 classified as correct, the applicant's analysis
14 spoke to a healthcare provider before the event of
15 abdominal pain. The FDA analysis resulted in only
16 one-third of participants who spoke to a healthcare
17 provider about sudden and severe abdominal pain.

18 This slide displays secondary endpoints for
19 which there was a high level of uncertainty. The
20 reason for the difference between the applicant
21 analysis and FDA analysis are displayed in
22 table 30, in Section 5.14.1, in the appendix of the

1 briefing document. I will highlight secondary
2 endpoint E, which tests the proportion of pack
3 transitions, where the participant did not report a
4 break between packs, and there were insufficient
5 data to draw conclusions because this analysis
6 includes the dosing data, with a large proportion
7 of participants, for the probable dosing in the
8 study.

9 I will also highlight secondary endpoint H,
10 which measured adherence to drug-drug interaction
11 warnings in the DFL, which directs consumers to ask
12 a doctor or pharmacist before use if they're taking
13 an interacting drug. Because the timing was not
14 reported in the verbatims as to whether
15 participants spoke to a healthcare provider before
16 use of the drug, there were insufficient data to
17 draw a conclusion on this endpoint.

18 This slide displays the results for the
19 secondary endpoints that assess adherence to taking
20 the tablet every day and at the same time every
21 day, accounting for mitigating behaviors. The
22 definition of a mitigating behavior is at the

1 footnote of the table on the slide. These
2 endpoints also have results with a high level of
3 uncertainty primarily due to the magnitude of
4 improbable dosing in the ACCESS population, but
5 also because information on sexual activity was not
6 obtained in participants less than 18 years old;
7 and therefore, these results regarding performance
8 and mitigating behaviors in the setting of a late
9 or missed tablet cannot be extrapolated to the
10 adolescent population.

11 This slide illustrates the marked difference
12 seen depending on how one analyzes the impact of
13 improbable dosing. When one classifies
14 participants who overreported as incorrect as a
15 method to explore range of assumptions, these
16 endpoints involving correct timing of dosing and
17 correct responses to the missed doses go from
18 correct response rates in the 90s to the 60s.

19 An issue for discussion that was not a
20 prespecified endpoint is abnormal vaginal bleeding
21 of undiagnosed etiology. There are 34 participants
22 who reported unexplained vaginal bleeding between

1 periods who entered the use phase of ACCESS.
2 Information on the number of participants who
3 reported these symptoms and spoke to a healthcare
4 professional was collected at the enrollment and
5 end-of-study interviews. There were
6 34 participants who reported unexplained vaginal
7 bleeding between periods who entered the use phase,
8 and based on classification of the verbatims by the
9 FDA review team, about 27 percent of participants
10 did not report speaking to a healthcare provider at
11 the enrollment interview, which was before use of
12 the product. Off-label use was noted by 24
13 participants in the study, most of whom are under
14 age 18. Reasons given for why these participants
15 used the drug off label included use to regulate
16 menstrual cycles, relieve menstrual symptoms, or
17 treat acne.

18 Next, I will be discussing the adverse
19 events in the ACCESS study and the postmarket
20 safety data. There were no deaths in the ACCESS
21 study. There were four serious adverse events.
22 One event of note was a thromboembolic event for

1 which causality could not be established.
2 Seven percent of participants reported
3 discontinuing the drug due to adverse events, and
4 approximately half of the participants who
5 discontinued the drug due to an adverse event did
6 so due to bleeding irregularities, which was the
7 most common category of adverse events overall.

8 Overall, there were no new safety signals
9 based on the data in the actual use study.

10 Regarding postmarketing adverse events, FDA
11 reviewed the data for multiple postmarketing
12 adverse event databases and a literature search,
13 and did not note conclusive data and specific
14 safety concerns.

15 This next section will highlight the actual
16 use study conclusions. In conclusion, the
17 magnitude of improbable dosing in the ACCESS study
18 raises concerns regarding the adequacy of evidence
19 in the actual use study. The reasons why
20 improbable dosing occurred are not evident, and the
21 root cause of improbable dosing are unknown. In
22 regards to the adolescent population in ACCESS,

1 there was a limited representation of younger
2 adolescents in the actual use study. Data on
3 sexual activity were not collected in adolescents,
4 and therefore, the number of adolescents that were
5 at risk for pregnancy is unknown.

6 Almost half of the participants reported
7 concomitant use of another hormonal contraceptive
8 for adolescents, and over 80 percent of
9 participants reported off-label use for
10 adolescents, which brings up the question of
11 whether there is adequate evidence of safe and
12 correct use in this population.

13 There was a greater proportion of
14 participants who were limited literacy and
15 improbable dosing group, which raises concerns
16 about the adequacy of evidence for adherence in
17 this population. The proportion of participants
18 that were limited literacy in the ACCESS study was
19 also well below representation in the U.S.
20 population. Although the majority of the
21 participants with unexplained vaginal bleeding
22 reported speaking to a healthcare provider before

1 use of the product, one-quarter did not report
2 speaking to a healthcare provider at the study
3 enrollment interview about this condition, which
4 raises the question of whether there is evidence of
5 safe use in participants with unexplained vaginal
6 bleeding.

7 The issues outlined in these slides are
8 among the key issues that FDA has identified for
9 the advisory committee to consider. Thank you for
10 your time, and that concludes my presentation.

11 **FDA Presentation - Pamela Horn**

12 DR. HORN: Thank you to all our presenters
13 and to all of you for your attention. In the next
14 few slides, I'm going to provide a summary of the
15 study findings as they relate to expected
16 effectiveness and safety of norgestrel tablet in
17 the nonprescription setting.

18 As we have heard, it was estimated at the
19 time of the 1973 approval that the likelihood of
20 becoming pregnant during one year of use of
21 norgestrel tablet was around 2 percent. Because of
22 population and study design differences, if studies

1 were conducted now, the efficacy estimate could be
2 quite different. The proposed population and
3 indication for this switch application are the same
4 as the approved product, and we want the discussion
5 today to focus on what we can expect in terms of
6 effectiveness of norgestrel in a nonprescription
7 setting.

8 To inform what effectiveness of norgestrel
9 tablet would be expected to be like in a
10 nonprescription setting, the applicant submitted
11 ACCESS, an actual use study, and collected
12 pregnancy outcome data, e-diary use data as
13 reported by the users in the study, and data on
14 whether consumers adhered to the drug interaction
15 DFL message from that study. In addition, the
16 applicant submitted comprehension data on the use
17 statements contained in the Drug Facts Label and
18 Consumer Information Leaflet from label
19 comprehension studies.

20 The sources of data were of varying
21 robustness to inform effectiveness in the
22 application. In this table, the left column lists

1 supportive evidence of likely effective use, which
2 comes from the comprehension data on directions for
3 use statements in the DFL and the Pearl Index
4 estimate from the ACCESS study, which yielded an
5 estimated likelihood of becoming pregnant during
6 one year of use of 2 to 6 percent. Of note, these
7 data came from a study with many design differences
8 and much less exposure than a typical contraceptive
9 efficacy study, and there were no pregnancy test
10 results for more than half of the study population.

11 Evidence that was not supportive of likely
12 effective use came from low comprehension of
13 statements in the labeling pertaining to emergency
14 contraception and when to use backup methods of
15 contraception, and low comprehension of drug
16 interaction statements that could decrease
17 norgestrel effectiveness. There are a number of
18 uncertainties related to likely effective use,
19 including that the risk of pregnancy in adolescents
20 was not known in the ACCESS study.

21 Consumers with limited literacy were
22 underrepresented in the actual use study;

1 unreliability of some of the self-reported e-diary
2 use data used to calculate adherence; and unclear
3 reliability of the use data overall. Pregnancy
4 test results are unknown in most access
5 participants, which again greatly limits the
6 interpretation of the Pearl Index estimate, and
7 there was not adequate documentation in the ACCESS
8 study to assess actual adherence to the label
9 statements about drug interactions. With respect
10 to safety, there's an agency finding of safety from
11 the original application approval, and no changes
12 are proposed to the population or indication in
13 this supplement.

14 To support that consumers would be able to
15 safely use and appropriately deselect from use, the
16 applicant submitted self-selection data from the
17 ACCESS and targeted breast cancer self-selection
18 study; self-reported use data and adverse event
19 data from the access study; and data on
20 comprehension of safety statements in labeling from
21 label comprehension studies.

22 Regarding the main safety issues FDA

1 identified in our review, data submitted are mixed
2 for the likelihood of correct deselection in
3 consumers with progestin-sensitive cancer. The
4 results of the targeted breast cancer
5 self-selection study were supportive overall, but
6 consumers with limited literacy were very
7 underrepresented, which limits the generalizability
8 of the results in comprehension of relevant label
9 statements in the label comprehension study, and
10 the occurrence of incorrect deselection in ACCESS
11 were not supportive of the likelihood of correct
12 deselection.

13 Next, there were multiple sources of
14 information in the application that indicates that
15 the messages relevant to abnormal vaginal bleeding
16 of undiagnosed etiology were not well understood.
17 The evidence provided in the application about use
18 with another hormonal contraceptive was generally
19 supportive of likelihood of adherence to the
20 do-not-use message.

21 With respect to adolescents, there are
22 uncertainties with respect to risks to bone health

1 in this subpopulation, and there are many unknowns
2 with respect to the likelihood of off-label use due
3 to a lack of information about sexual history and
4 risk of pregnancy in the application for this
5 subpopulation.

6 For the limited literacy subpopulation,
7 there are uncertainties about safe use due to
8 underrepresentation in some of the submitted
9 studies and challenges in generalizing the
10 submitted data to this target population, which
11 will include consumers with limited literacy.

12 In conclusion, the evidence for likelihood
13 of effectiveness in the nonprescription setting
14 submitted by the applicant is mixed and has many
15 limitations, especially with respect to the data
16 submitted from the ACCESS study, where the
17 uncertain reliability of the self-reported actual
18 use data presents major challenges in interpreting
19 the study results.

20 With respect to the evidence of the
21 likelihood of appropriate deselection and correct
22 actions based on the proposed labeling, where there

1 are potentially serious clinical consequences of
2 incorrect deselection for use, the evidence in
3 consumers with progestin-sensitive cancer is mixed,
4 and the evidence related to abnormal vaginal
5 bleeding of undiagnosed etiology is generally not
6 supportive of safe use.

7 Finally, there is most uncertainty in the
8 evidence to support likelihood of safe and
9 effective use in the adolescent and limited
10 literacy subpopulations of consumers, and thus, we
11 would like the committee to focus their discussion
12 on all of these issues when we get to the
13 discussion questions and voting question for the
14 committee tomorrow.

15 Thank you to all the FDA speakers and review
16 staff for your tireless efforts in conducting an
17 incredibly thoughtful and thorough evaluation of
18 this application. This concludes the FDA
19 presentations, and we will now move to clarifying
20 questions.

21 **Clarifying Questions**

22 DR. COYLE: Thank you.

1 We will now begin clarifying questions for
2 FDA. Please use the raise-hand icon to indicate
3 that you have a question, and remember to lower
4 your hand by clicking the raise-hand icon again
5 after you've asked your question. When
6 acknowledged, please remember to state your name
7 for the record before you speak -- and I'll provide
8 reminders as well -- and also to direct your
9 question to a specific presenter, if you can. If
10 you wish for a specific slide to be displayed,
11 please let us know the slide number, if possible.

12 Finally, it would be helpful to acknowledge
13 the end of your question with a thank you, and end
14 of your follow-up question with, "That is all for
15 my questions," so that we can move on to the next
16 panel member.

17 I'd like to go ahead and call on Dr. Shaw
18 for the first question.

19 DR. SHAW: Thank you. This is Pamela Shaw.
20 My question relates to the presentation of the
21 selection results for ACCESS perhaps around
22 slide 104, or maybe somewhere around 100.

1 My question relates to the question I had
2 earlier, which is, as I look at the presentations
3 from the sponsor and the FDA, you are analyzing a
4 different primary endpoint, in the sense that the
5 primary endpoint for selection from the FDA is
6 based on that question 1 on slide 99, and should
7 not include any purchase information.

8 As FDA mentioned, there's very clear
9 guidance, in the 2013 guidance for nonprescription
10 drugs, that purchase information should not be used
11 in the selection evaluation, but that the sponsor
12 is using purchase information to calculate a
13 primary endpoint. So what I see is that there are
14 two different primary endpoints in question here,
15 one presented by the sponsor and one presented by
16 the FDA.

17 I guess what I'm trying to understand is how
18 this happened. To what extent was this discussed
19 at the start of ACCESS or before it was conducted
20 versus after it was conducted, and all those women
21 who dedicated their time, the data is now a
22 question.

1 As a closely related question, there were a
2 lot of differences in how the data were counted as
3 success or a failure and how missing data was
4 treated, so I guess I'd like some understanding
5 about the ACCESS trial and the regulatory
6 environment informing the design of that trial.
7 Perhaps I'll stop there. I just really am quite
8 confused by the level of discrepancy and how data
9 was analyzed for this trial.

10 DR. HORN: Hi. This is Pamela Horn. I'm
11 going to start with our response. Thank you. I
12 think you had a few questions in there, so I'm
13 going to try to take them apart a little bit so my
14 colleagues can answer.

15 Let me refer the first part of your question
16 to Barbara Cohen. You had mentioned the guidance
17 and the difference in the analyses, and how FDA
18 views the self-selection analysis. We'll start
19 there, and then we'll move to your other ones.

20 MS. COHEN: This is Barbara Cohen, FDA.
21 Thank you very much for that important question
22 and, yes, the study was a complex one, so I

1 appreciate the opportunity to clarify it a bit
2 more.

3 I'll just start by saying that personally,
4 I've been at FDA since 2011. I have not ever seen
5 a self-selection study analyzed in this way. We
6 didn't discuss it in regulatory development because
7 we didn't know there was anything to discuss
8 per se. And when we received the application,
9 there was not really a clear mention of this made
10 either; that they had disagreed with the guidance
11 and that we're analyzing it in this way.

12 I'm just saying an applicant is free to
13 disagree with us, but we just didn't know
14 beforehand, so there was a limited opportunity for
15 discussion about it. The discussion happened, and
16 in the application itself, there was no mention of
17 the magnitude of how many people this affected, so
18 that was the other key elements of this.

19 Did that respond to the first question that
20 you asked?

21 DR. SHAW: Yes. I believe so. To clarify,
22 there are two reasons --

1 MS. COHEN: Yes.

2 DR. SHAW: -- for the sponsor's analysis to
3 be different. One is that they're using
4 questions 1 and 2 instead of question 1 alone, so
5 they're using --

6 MS. COHEN: Right.

7 DR. SHAW: -- this purchase information.

8 Then the other issue, there's clear
9 guidance, once you make this little table of
10 selectors and non-selectors, you can either do the
11 A over A plus B or the A plus D over A plus B ,
12 plus C , plus D . It even tells you how to do the
13 fraction, and even how they did the fraction was
14 different.

15 MS. COHEN: Yes.

16 DR. SHAW: So neither one of those things
17 was discussed because, typically, in your
18 experience, people just follow the guidance in the
19 nonprescription environments.

20 MS. COHEN: Yes. The equation for the
21 deselection endpoint we agree on, which is D over B
22 plus C .

1 DR. SHAW: Okay.

2 MS. COHEN: It's the equation for the
3 selection endpoint that we don't agree, yes.

4 DR. SHAW: Sorry. I misspoke on that. So
5 there are two things that seem to be different than
6 the guidance there.

7 MS. COHEN: Yes.

8 DR. SHAW: Okay. So that answered my
9 question. And I apologize; my question was
10 conflating a few things there because it is a
11 complex issue today, so I appreciate that first
12 question I think is answered now. Then I had some
13 follow-ups regarding other discrepancies, but I'll
14 turn it back to the FDA who thought they wanted to
15 unpack my question, other aspects of the -- [audio
16 feedback].

17 DR. HORN: Yes. This is Pamela Horn,
18 DNPD II director.

19 Would you mind following up and stating your
20 next part of your question again for us?

21 DR. SHAW: Yes. There are some other areas
22 of discrepancy. Say, for example, in the adherence

1 figures we just saw, relate to the handling of
2 missing data, and how to treat missing data or
3 whether to exclude it in a per protocol, or
4 thinking of worst case. There were other aspects
5 of the analysis -- that's just one example -- that
6 also seemed quite different than the FDA. Much of
7 the presentations are table after table of we
8 calculated it differently, so I'm just wondering
9 were there other aspects of the analysis related to
10 handling of missing data, or calculation, or the
11 design of the adherence trial that were discussed
12 in advance? Just again, wondering how we got such
13 discrepant pictures, say, of the adherence.

14 DR. HORN: Okay. Yes. Thank you, Dr. Shaw.
15 Pamela Horn, DNP II. Again, I'm going to ask
16 Dr. Murry to start the answer for that question
17 about regulatory interactions on the application.

18 DR. MURRY: In meetings that we hold with
19 applicants, or sponsors, prior to submission of
20 their application, we do discuss with them about
21 what to do regarding missing data, and we have
22 quite clear guidance on that.

1 Regarding the specific most dramatic
2 difference between the applicant's analyses and
3 FDA's analyses related to the improbable dosing, I
4 will let Dr. Zhang talk for a moment about the
5 decisions that were made regarding analyses there,
6 and then I'll have a little bit of clinical
7 follow-up after that.

8 DR. ZHANG: This is Rongmei Zhang,
9 mathematical statistician in the Division of
10 Biometrics VII. First of all, I want to say that,
11 in general, the per protocol analysis and
12 worst-case analysis, the applicant's and FDA's
13 definitions are the same, so we handled not taking
14 norgestrel differently in the evaluation of time of
15 dose, where the sponsor excluded them, but we
16 included them.

17 In terms of the sensitivity analysis and
18 analyzed improbable dosing, the FDA sensitivity
19 analysis evaluated the robustness of results based
20 on a range of assumptions. Our sensitivity
21 analysis, which assumed those with improbable
22 dosing did not take norgestrel, was intentionally

1 extreme. And as we said in our presentation, a
2 large proportion of participants with improbable
3 dosing raises concerns about accuracy of reporting
4 among participants who did not report taking more
5 tablets than dispensed. Also, intentional and
6 inadvertent overreporting may have occurred in
7 those without improbable dosing. So without good
8 information on the reasons for overreporting, we
9 have questions on the reliability of ACCESS use
10 data.

11 DR. MURRY: Thank you.

12 Karen Murry, deputy director,
13 nonprescription, again. Expanding on what
14 Dr. Zhang said from a clinical standpoint, when we
15 find data integrity problems, we routinely do
16 analyses such as these, and if the analysis shows
17 little statistical effect of assuming that the
18 participants with data integrity problems were
19 incorrect, that's comforting to us; and if that had
20 been the case here, the data integrity problems
21 might have been less concerning. However, that was
22 not the case for these analyses with these

1 participants, with the impossible result of
2 reporting taking more tablets than were dispensed.

3 I think for your overall question of the
4 frequent differences between the analyses presented
5 by the applicant and the analyses presented by FDA,
6 it does appear that the applicant frequently
7 included mitigations that would result in a more
8 favorable interpretation than FDA would have come
9 to using our usual methods of analysis. So I'll
10 stop there, and hopefully we've answered your
11 question there.

12 DR. SHAW: Thank you very much. I feel like
13 this discussion is helpful. I'd like to yield the
14 floor to others who have questions. Thank you.

15 DR. COYLE: Thank you, Dr. Shaw.

16 I'm going to go ahead and call on Dr. Leslie
17 Walker-Harding.

18 DR. WALKER-HARDING: Hello. Leslie
19 Walker-Harding. I don't remember the slide, but in
20 terms of adolescents, one of the questions I had
21 was, do you have information on their prior
22 knowledge before they had used contraceptives prior

1 to this study? Because a lot of the things that
2 I'm hearing sound like they might have been more
3 educated users, especially around the irregular
4 bleeding, where that's the first-line treatment
5 usually for adolescents, would be to use oral
6 contraceptives, progestin-only or with estrogen.

7 Then with the kids who used two kinds of
8 contraceptives, again, were they talking to their
9 providers? Did they know that, yes, in fact that's
10 what you might do if you had spotting, and that was
11 concerning to you; that you might use a second -- I
12 mean, that's what gets prescribed, is the second
13 contraceptive to sometimes help the spotting.

14 I'm curious about if there's any information
15 on the knowledge of the adolescents prior to
16 beginning this, or the amount of times they might
17 have talked or looked up how to treat certain
18 things on their own.

19 DR. HORN: Thank you, Dr. Walker-Harding.
20 This is Pamela Horn, DNP II. I'm going to ask
21 Dr. Jacob to start the response to that question
22 regarding what we know about the adolescent

1 subpopulation in the ACCESS study, and what
2 information we had about them prior to study entry.

3 DR. JACOB: Thank you. Jeena Jacob, medical
4 officer, Division of Nonprescription Drugs. We do
5 have information available on how many adolescents
6 experienced unexplained vaginal bleeding prior to
7 starting the product. We also have information on
8 the participants that were on other hormonal birth
9 control products, but we don't have any specific
10 information on whether they used other hormonal
11 birth control products in the setting of the
12 vaginal bleeding. They may have used other hormonal
13 birth control products prior to experiencing
14 vaginal bleeding, but we don't have information on
15 the time course of those events.

16 DR. HORN: And does that answer your
17 question, or did you have a follow-up?

18 DR. WALKER-HARDING: No. That's good.
19 Adolescents tend to have something that they would
20 call unexplained vaginal bleeding pretty commonly,
21 so I was curious what the understanding of their
22 knowledge was. That's good. Thank you, if you

1 don't have the information.

2 DR. COYLE: Thank you, Dr. Walker-Harding.

3 I'll go ahead and call on our next speaker,
4 Dr. Berlan.

5 DR. BERLAN: Hi there. Thanks. This is
6 Elise Berlan, Ohio State University, Nationwide
7 Children's Hospital. I had a question about the
8 improbable dosing. I think this would go to
9 Dr. Jacob, and I'm looking at slide 134.

10 My question is I don't recall seeing any
11 data around the magnitude of improbable dosing and
12 the distribution of improbable dosing among the
13 population that reported improbable dosing, and if
14 you could comment on that, I would appreciate it.
15 Thank you.

16 DR. JACOB: Thank you. Jeena Jacob, again,
17 medical officer, DNP II. That's a really great
18 question. One of our concerns is about the
19 magnitude of improbable dosing in the user
20 population. In terms of the participants that had
21 improbable dosing, about 50 percent reported in
22 excess of 29 tablets or greater, and about

1 10 percent of the improbable dosing population
2 reported in excess of 113 tablets or greater.
3 There were also 2 participants who reported in
4 excess of 500 tablets, one of which reported close
5 to 700 tablets. So our concern is really not only
6 how prevalent improbable dosing was in the user
7 population, but the magnitude.

8 DR. COYLE: Did that address your question?

9 DR. BERLAN: Yes. Thank you.

10 DR. COYLE: Thank you.

11 And just as a reminder, when you've heard a
12 response that satisfies your question to all of our
13 advisory committee members, please do go ahead and
14 indicate that you have sufficient information so
15 that we can easily move on to the next individual.

16 I would like to do that now and acknowledge
17 Ms. Robotti with her question.

18 MS. ROBOTTI: Hello. Thank you. It's
19 Suzanne Robotti. I have two questions. One is
20 very easy. I'm not a doctor, so could somebody
21 please very quickly explain to me what is the
22 physical harm or risk of using the Opill; or if the

1 use of the Opill overlaps with another hormone
2 method for a limited period of time, like
3 1 to 5 days, another birth control pill; or if it's
4 used within 5 days as emergency contraception? Of
5 course, I'm asking that because there was limited
6 understanding, and I want to know what risk is
7 happening then.

8 DR. KOTAK: This is Anandi Kotak, medical
9 officer, Division of Urology, Obstetrics, and
10 Gynecology. Thank you so much for your question,
11 and as you indicated, concomitant use with other
12 hormonal contraceptives by themselves does not pose
13 a risk to the health of the individual. The
14 concern is whether or not the individual is
15 understanding the directions for use and how to
16 switch to another contraceptive method. So our
17 concern when we see that individuals in the ACCESS
18 use phase of the study were using two sets of
19 contraceptives at the same time, did they really
20 understand why they were using Opill?

21 With regard to ulipristal acetate emergency
22 contraception, the efficacy of norgestrel can be

1 reduced by using ulipristal acetate up to 5 days
2 prior to starting norgestrel use. So the concern
3 is reduced efficacy of norgestrel and, vice versa,
4 that norgestrel can reduce the efficacy of
5 ulipristal acetate. So there is the concern for
6 unintended pregnancy. That would be the harm that
7 we're concerned about.

8 MS. ROBOTTI: Thank you.

9 The next question, I believe, is Dr. Jacob
10 in slide 152. I'm going back to improbable use,
11 both for taking the tablets and for taking them at
12 the same time each day. Do we have comparison data
13 for prescribed oral contraception? Is there any
14 research on how much women comprehend after an
15 in-person visit? I feel like we need a comparison
16 group. The results of the comprehension study
17 don't look great, but on an objective level, how
18 much better or worse are they?

19 DR. HORN: This is Pamela Horn, DNP II.
20 Thanks for that question. I just want to make sure
21 that we understand exactly what you're asking.

22 Could you just restate exactly what it is

1 that you would like to know about prescription use?

2 MS. ROBOTTI: Well, in listening to the FDA
3 discuss -- I believe it was -- slide 152 around
4 that area, it was talking about -- maybe that's not
5 the right slide to go to, but the entire question
6 of what do women comprehend from reading the
7 package?

8 Is there comparator information to what
9 women comprehend after being prescribed an oral
10 contraceptive? Do 90 percent of the women walk out
11 of the office knowing exactly what they're supposed
12 to know, or is it 85 percent, or is it 72 percent?
13 And how is the literacy? I assume it's more
14 comprehensible. I'm not sure. How do we know?

15 DR. HORN: Okay. Yes. Thank you. Pamela
16 Horn, DNP II. I think the brief answer that I'll
17 start with is those are not studies that are
18 typically done in the prescription setting for
19 prescription drug approvals. I think the short
20 answer would be that we would not have that data
21 for a prescription drug application.

22 I'm going to pause for a second and see if

1 any of my colleagues from DUOG have anything to add
2 to that.

3 Dr. Nguyen?

4 DR. NGUYEN: Hi. Thank you. Christine
5 Nguyen, deputy director in the Office of Rare
6 Diseases, Pediatrics, Urologic, and Reproductive
7 Medicine. That's really an excellent question. We
8 don't really have data on the adherence rates in
9 the prescription setting.

10 One thing that I would like to emphasize
11 that I think is really important is that in a
12 prescription setting, as Dr. Kotak mentioned early
13 in her presentation, we prescribe progesterone-only
14 pills to select patients. These are highly curated
15 patients, mostly breastfeeding patients or those
16 who either can't use estrogen or don't want to use
17 estrogen, so usually pretty highly motivated,
18 highly compliant individuals. So it's really
19 difficult to extrapolate the data that we have
20 under the Rx setting to a more general consumer
21 population for which would be an OTC setting. And
22 that's true even for the actual use pregnancy rates

1 that's published out there, so I'll ask everyone to
2 keep that in mind. Thanks.

3 MS. ROBOTTI: Thank you. That answers my
4 questions.

5 DR. MURRY: Karen Murry, deputy director,
6 Office of Nonprescription Drugs. That segues
7 nicely into an explanatory statement that we need
8 to make regarding some things that were said this
9 morning.

10 It's important to note that nonprescription
11 means something different in the U.S. than it means
12 in most of the rest of the world, including the
13 vast majority of the quoted over 100 countries in
14 which women can get a routine oral contraceptive
15 without a physician's prescription. In the U.S.,
16 we only have two types of drugs, prescription and
17 nonprescription. Here, prescription means no
18 healthcare professional is involved. In other
19 countries, there's often a third category of
20 pharmacist-dispensed, and in that case, while the
21 consumer might not have a physician's prescription
22 for the product, they still have to talk to a

1 pharmacist who may or may not dispense the product
2 after talking to and often counseling the consumer.

3 Pharmacists are definitely highly trained
4 healthcare professionals, and in the U.S., we don't
5 have that legal third category of drugs. Here,
6 there will be no such interaction, and if this
7 product is approved, people might get it in a
8 pharmacy, but they also might get it in a gas
9 station or a big-box store with no healthcare
10 professionals around. Therefore, FDA can't really
11 rely on the experience in those other countries to
12 truly inform what would happen in the situation of
13 wide open, unrestricted access in the U.S., and I
14 don't want the advisory committee to be misled into
15 thinking that over 100 countries have
16 nonprescription status equivalent to what would
17 occur in the U.S. In fact, very few countries do.

18 DR. COYLE: Thank you, and thank you for
19 those clarifying remarks.

20 I'm going to move on in the interest of time
21 to Dr. Fox.

22 DR. FOX: Hi. Good afternoon. I wanted to

1 ask --

2 DR. COYLE: And could you please say your
3 full name for the record? Could you please state
4 your name?

5 DR. FOX: Sure. Hi. Good afternoon. I'm
6 Michelle Fox. I'm the industry representative on
7 the panel. While I understand the concern about
8 the 30 percent of participants who had somewhat
9 significant reports of overuse, I'm not
10 understanding why this is calling into question the
11 70 percent that had no such actions.

12 It's my understanding that even in recent
13 contraceptive applications for prescriptions, paper
14 diaries were still acceptable to document whether
15 or not pills were taken, and paper diaries, as we
16 all know, have a lot more limitations than any
17 electronic diaries. So I'm not understanding why
18 we are calling into question the majority of the
19 data that was submitted because of some unclear
20 behaviors of certain participants, especially since
21 when those participants are excluded, the
22 sensitivity analyses seem to come up with the same

1 results.

2 DR. HORN: Hi. This is Pamela Horn,
3 DNP II. Thank you for that question. I think
4 that our concern about being able to rely on the
5 data in the study overall comes from the fact that
6 we don't have an understanding of why people
7 overreported in 30 percent of the study population.
8 If we felt confident we understood what happened
9 there, I think that would perhaps change the
10 picture for us, but we don't have an understanding
11 of that; and there's potentially only a difference
12 of whether someone overreported just less than the
13 number that they were dispensed or just more than
14 they were dispensed between the improbable dosing
15 group and the rest of the study participants, which
16 I think we could say that that's sort of an
17 artificial line to draw when we're talking about
18 trying to understand actual adherence.

19 DR. COYLE: Dr. Fox, did that address your
20 question?

21 DR. FOX: Well, it addresses the first part.
22 I'm still confused as to if paper diaries, that

1 have no such ability to track reliability, are
2 still acceptable, why it is such a concern about
3 this electronic diary in the patients who have no
4 reports, no obvious issues.

5 DR. HORN: Hi. This is Pamela Horn,
6 DNPD II, again. I'll try to start our answer to
7 that as well. I'm going to let my colleagues speak
8 about the purpose of the paper diary in
9 prescription applications.

10 I will note that the purpose of the e-diary
11 in this study is likely different. What we're
12 trying to ascertain in an actual use study is
13 whether the understanding that was assessed in a
14 label comprehension study translates into behavior
15 for participants in a naturalistic setting. That
16 goal is quite different than the goals of studies
17 in the prescription setting.

18 I'm going to ask if anybody else wants to
19 comment.

20 Dr. Michele?

21 DR. MICHELE: Hi. This is Dr. Theresa
22 Michele, director of the Office of Nonprescription

1 Drugs. I think that's a really profound kind of
2 question to ask, and one that we've asked ourselves
3 quite a lot with this.

4 I just wanted to note that this finding of
5 improbable dosing in this study is really quite
6 extraordinary. This is not something we see in a
7 typical actual use study, and the results have to
8 be incredibly extreme to show up in this kind of a
9 study because we're really looking at a very blunt
10 instrument for determining this finding.

11 In order for us to pick up on the fact that
12 consumers were reporting doses that they didn't
13 take, they had to way overreport to the point where
14 they were reporting dosing beyond the number of
15 tablets that they received. So if we got that
16 result in 30 percent -- that's almost a third of
17 the subjects in the trial -- you really have to
18 wonder about what happened with the other
19 two-thirds, if they also overreported, but just not
20 to the extent where we could pick up on it. So
21 that's the question that we're asking the advisory
22 committee to ask themselves, which is what we've

1 spent quite a lot of time asking ourselves as we
2 consider this. Thank you.

3 DR. FOX: Thank you. That answers my
4 question.

5 DR. COYLE: Thank you.

6 I think we will go ahead and take a break at
7 this point. We need to stay true to our schedule
8 since it is quite full. We will take names down,
9 so if you did not have a chance to ask your
10 question, and we have some room in the agenda later
11 on, we will return to those, so please make note of
12 it.

13 At this point, we will take a quick
14 15-minute break. Panel members, please remember
15 that there should be no chatting or discussion of
16 the meeting topic with other panel members during
17 this time, and we'll reconvene at 3:45 p.m. Eastern
18 Time. Thank you.

19 (Whereupon, at 3:33 p.m., a recess was taken,
20 and meeting resumed at 3:45 p.m.)

21 **Open Public Hearing**

22 DR. COYLE: We will now begin the open public

1 hearing session.

2 Both the FDA and the public believe in a
3 transparent process for information gathering and
4 decision making. To ensure such transparency at
5 the open public hearing of the advisory committee
6 meeting, FDA believes that it is important to
7 understand the context of an individual's
8 presentation.

9 For this reason, FDA encourages you, the
10 open public hearing speaker, at the beginning of
11 your written or oral statement to advise the
12 committee of any financial relationship that you
13 may have with the applicant, its product, and if
14 known, its direct competitors. For example, this
15 financial information may include the applicant's
16 payment of your travel, lodging, or other expenses
17 in connection with your participation in this
18 meeting.

19 Likewise, FDA encourages you, at the
20 beginning of your statement, to advise the
21 committee if you do not have any such financial
22 relationships. If you choose not to address this

1 issue of financial relationships at the beginning
2 of your statement, it will not preclude you from
3 speaking.

4 The FDA and this committee place great
5 importance in the open public hearing process. The
6 insights and comments provided can help the agency
7 and this committee in their consideration of the
8 issues before them.

9 That said, in many instances and for many
10 topics, there will be a variety of opinions. One
11 of our goals for today is for this open public
12 hearing to be conducted in a fair and open way,
13 where every participant is listened to carefully
14 and treated with dignity, courtesy, and respect.
15 Therefore, please only speak when recognized by the
16 chairperson. Thank you for your cooperation.

17 Speaker number 1, please unmute and turn on
18 your webcam. Will speaker number 1 begin and
19 introduce yourself? Please state your name and any
20 organization you are representing, for the record.

21 DR. BRANDI: Good afternoon. My name is
22 Dr. Kristyn Brandi. I use she or her pronouns. I

1 am also a cisgendered woman of reproductive
2 potential who has benefited from accessing
3 contraception for my entire adult life. I'm an
4 obstetrician/gynecologist with fellowship training
5 in complex family planning and a master's in public
6 health. I have no conflicts of interest to
7 disclose.

8 I currently serve as the Darney-Landy fellow
9 for the American College of Obstetricians and
10 Gynecologists, or ACOG, representing over
11 60,000 members to provide evidence-based obstetric
12 and gynecological care. ACOG thanks the FDA for
13 holding today's meeting and for the opportunity to
14 offer comments. Based on today's safety data and
15 the known benefits of contraception, ACOG
16 whole-heartedly supports over-the-counter access to
17 progestin-only pills, or POPs, without age
18 restriction. On behalf of ACOG, I'd like to speak
19 briefly on the following points.

20 Number one, people seeking contraception
21 face obstacles. These hurdles include cost
22 barriers, challenges obtaining an appointment, a

1 clinician incorrectly requiring an office visit or
2 a lack of a regular clinician, and difficulty
3 accessing a pharmacy. People from marginalized
4 communities, including racial and ethnic
5 minorities, uninsured people, and those who don't
6 speak English, are more likely to face these
7 barriers. Young people especially face barriers to
8 access contraception, and this can lead to delays,
9 and for others, it may mean that they never access
10 contraception. I want to underscore again that
11 ACOG supports over-the-counter access to hormonal
12 contraception without age restrictions.

13 Number two, hormonal contraception,
14 including POPs, are safe. The CDC asserts that the
15 advantages generally outweigh theoretical or proven
16 risks for POPs for an individual with nearly any
17 comorbidity, and POPs can be used for women of all
18 ages. This includes people with obesity who, based
19 on the data, can effectively and safely use POPs.
20 Patients of all ages with comorbidities are already
21 safely using these methods by prescription.

22 The data are clear that progestin-only

1 hormonal methods are safe and carry no or minimal
2 risks of venous thromboembolism, or VTE, especially
3 when considering the risk of VTE in pregnancy in
4 the postpartum period. Evidence also shows that
5 all prescription contraceptives, including POPs,
6 are protective of ectopic pregnancy.

7 Number three, people can effectively
8 self-screen for contraindications. Despite the
9 safety of oral contraceptives, I've heard concerns
10 raised about contraindications. Only current
11 breast cancer is considered a condition that
12 represents an unacceptable health risk for POPs.
13 Data show that the prevalence of relative and
14 absolute contraindications for POPs amongst women
15 of reproductive age are incredibly low. Evidence
16 is also clear in supporting people that can
17 accurately self-screen, including people that are
18 young.

19 The scientific evidence is clear;
20 over-the-counter access to contraception without
21 age restrictions can be accomplished safely. The
22 benefit of increase access is significant. We at

1 ACOG trust patients of all ages to make their own
2 decisions about what's best for their health,
3 including taking over-the-counter POPs. We
4 encourage the FDA to review the robust evidence
5 supporting the safety and efficacy of the
6 over-the-counter POPs, and to make a decision
7 that's grounded in science. Thank you for your
8 time.

9 DR. COYLE: Speaker number 2, please unmute
10 and turn on your webcam. Will speaker number 2
11 begin and introduce yourself? Please state your
12 name and any organization you are representing, for
13 the record.

14 MS. PHILLIPS: Hi. I am Sophia Phillips,
15 speaking on behalf of the National Center for
16 Health Research. We are a nonprofit think-tank
17 that studies the safety and effectiveness of
18 medical products. We do not accept funding from
19 companies that make those products, so we have no
20 conflicts of interest.

21 Since girls and women who are prescribed
22 birth control pills don't always take them daily or

1 at the same time every day, we do not think that is
2 an issue of greater concern regarding
3 over-the-counter access to norgestrel or Opill.
4 Instead, we'll focus on other types of imperfect
5 use shown by the data.

6 We are concerned that if birth control pills
7 become available over the counter, preteens and
8 young teens may use them inappropriately. We agree
9 with FDA scientists that the ACCESS study data
10 can't be generalized for preteens since only
11 3 participants were 12 and none were younger. Only
12 49 girls were younger than 15, and the applicant
13 did not collect information on sexual history at
14 enrollment or sexual activity during the study, so
15 we don't know if they abstained from sex or use
16 barrier contraception when they initiated use of
17 Opill or after missing a pill.

18 Young adolescents demonstrated especially
19 low comprehension of certain key messages, like the
20 need for additional non-hormonal contraception when
21 starting the drug or after missing a dose. They
22 also scored low in understanding of do not use as

1 an emergency contraceptive.

2 The ACCESS UP study showed improbable dosing
3 results for approximately one-third of
4 participants, and two-thirds of those individuals
5 reported over 20 percent more doses than their
6 available supply. This calls into question the
7 reliability of the actual use data.

8 We agree with the FDA that even with the
9 do-not-use warning, we should be concerned about
10 the lack of comprehension of women who have or ever
11 had breast cancer. Although, few breast cancer
12 patients use birth control pills, and most properly
13 deselected from taking Opill, the data may not be
14 generalizable to the real world since participants
15 were not given the option of actually taking Opill,
16 and very few had limited literacy.

17 Similarly, in the ACCESS SSP study, more
18 than half of the participants who initially stated
19 that they had unexplained vaginal bleeding and had
20 not discussed it with their doctor, incorrectly
21 decided that Opill would be appropriate for them to
22 use. A quarter of participants in the ACCESS UP

1 study also reported that they had not spoken to a
2 healthcare professional about their unexplained
3 bleeding before or at any time during the study.
4 Although they did not experience significant side
5 effects during the study, this shows a lack of
6 understanding of the risks and a failure to seek
7 medical advice or appropriately desist from using
8 Opill.

9 FDA asked that one-third of study
10 participants should have limited literacy. The
11 breast cancer self-selection study and ACCESS
12 studies had far fewer participants with limited
13 literacy. Although it's challenging to recruit
14 participants with limited literacy, FDA's request
15 was important so that the results would be
16 generalizable to the expected consumer population.

17 Finally, while only 1 percent of
18 participants used Opill --

19 DR. COYLE: Please consider wrapping up.
20 You're out of time.

21 MS. PHILLIPS: Sure.

22 We urge this panel to consider these

1 concerns and whether they can be addressed if Opill
2 is sold over the counter. Thank you.

3 DR. COYLE: Thank you.

4 Speaker number 3, please unmute and turn on
5 your webcam. Will speaker number 3 begin and
6 introduce yourself? Please state your name and any
7 organization you are representing, for the record.

8 MR. DOWNING: Good afternoon, committee
9 members. My name is Don Downing, and I have no
10 financial relationships to disclose. I'm a
11 pharmacist and clinical professor of pharmacy at
12 the University of Washington in Seattle, and I will
13 speak to my support for FDA OTC approval of Opill.

14 I have spent years reimagining how people
15 access healthcare services, namely by unmasking
16 unnecessary barriers to care and developing novel
17 ways to meet people's health needs. This includes
18 helping to develop Plan B, creating the nation's
19 first Self-Determination Act tribal healthcare
20 clinic, and developing the nation's first community
21 pharmacy vaccination programs.

22 In 1998, when emergency contraception

1 required prescribing a few doses of regular birth
2 control pills, our pharmacy team in Washington
3 State was concerned about the very few people who
4 were able to access emergency contraception through
5 traditional care. During the prior two years, just
6 2500 people per year were able to access emergency
7 contraception in Washington State. In response, we
8 modeled direct access to contraception in
9 pharmacies.

10 Contraceptive access was available during
11 evenings, the weekends, and holidays, times when
12 many consumers have some free time but when
13 traditional medical clinics are often closed.
14 Within 6 months of starting this direct access
15 model, pharmacists in our state began seeing more
16 than 2500 women every month for emergency
17 contraception compared to the 2500 people per year
18 using traditional models.

19 Our project proposed that 2[00] or
20 3[00] people would see us in the first 6 months,
21 but instead we saw nearly 12,000. We found that
22 when community pharmacies provided OTC-like access

1 to contraception, we were also uncovering a massive
2 unmet need. This need had been masked by the many
3 barriers that traditional care models had created.
4 People, especially those who could ill afford to
5 miss work, were now accessing contraception without
6 taking time off from work or school, but rather on
7 their own terms and on their own schedules.

8 Not all states permit direct access to
9 contraception in pharmacies, and we need to find a
10 way where consumers in every state can more easily
11 access contraception. Therefore, I look forward to
12 us breaking barriers to care through the approval
13 of Opill as an FDA-approved OTC contraceptive. The
14 existing barriers are certainly not just a matter
15 of inconvenience; they are critical to people's
16 ability to access the safety that they seek and
17 need. Thank you very much.

18 DR. COYLE: Thank you.

19 Speaker number 4, please unmute and turn on
20 your webcam. Will speaker number 4 begin and
21 introduce yourself? Please state your name and any
22 organization that you are representing, for the

1 record.

2 MR. SPANGLER: Good afternoon. I'm David
3 Spangler with the Consumer Healthcare Products
4 Association. We represent and are funded by over
5 65 manufacturers of nonprescription or OTC
6 medicines, dietary supplements, and consumer
7 medical devices, including HRA Pharma through
8 Perrigo.

9 As I stressed the last time I spoke to the
10 Nonprescription Drugs Advisory Committee, access
11 matters. Access is about removing barriers, and
12 when it comes to oral contraceptive pills, already
13 among the most common contraceptive methods used by
14 women, OTC availability will, simply put, increase
15 access.

16 The leading cause of unintended pregnancy is
17 inconsistent or lack of contraceptive use. As the
18 sponsor highlighted, among the 40 million women who
19 want to avoid pregnancy, more than a third of them
20 are either not using a contraceptive method or
21 using a contraceptive method CDC classifies as less
22 effective. An OTC oral contraceptive will increase

1 their options. OTC access facilitates a broader
2 more constant supply by removing steps and
3 increasing availability of access points. A 2015
4 study by Foster and others found over a fifth of
5 low-income women at risk for unintended pregnancy
6 were very likely to use oral contraceptive pills if
7 they were available without a prescription.
8 Neither CHPA nor HRA Pharma funded this study.

9 I'm well aware it is not FDA's role to base
10 its decisions on economic considerations, but as
11 part of larger society, I want to raise one point
12 in the economic realm. The Kaiser Family
13 Foundation reports 11 percent of women ages
14 19 to 64 are uninsured. Those women often have
15 inadequate access to care and get a lower standard
16 of care when they are in the health system. If
17 access matters to all of us, it certainly matters
18 to those individuals; and overall, every dollar
19 spent on new OTCs yields over 7 dollars in health
20 system benefits.

21 Where does this leave us? 1) the sponsor's
22 presentation and studies by others show women are

1 interested in an OTC oral contraceptive option;
2 2) they want better access; 3) unintended
3 pregnancies are high; 4) the Food, Drug, and
4 Cosmetic Act does not include comparative
5 effectiveness versus other drugs as a criterion,
6 and as a corollary to that, one wouldn't expect a
7 supplemental new drug application to have to
8 reprove effectiveness of the original new drug
9 application; fifth, more access for more women to
10 meet their reproductive health needs is a means to
11 help.

12 DR. COYLE: Thank you.

13 Speaker number 5, please unmute and turn on
14 your webcam. Speaker number 5, please begin and
15 introduce yourself. Please state your name and any
16 organization you are representing, for the record.

17 DR. DAVIES: Hi. Thank you so much, and
18 good afternoon. My name is Shelby Davies. I'm a
19 pediatrician, and speaking to you on behalf of the
20 North American Society for Pediatric and Adolescent
21 Gynecology, or NASPAG, which is a leading
22 organization dedicated to multidisciplinary

1 collaborations in education, research, and
2 gynecologic care to improve the reproductive health
3 of youth.

4 NASPAG individually and in partnership with
5 organizations such as ACOG, AAP, and SAHM have
6 served as leaders in advocacy for unrestricted,
7 unbiased, and evidence-based reproductive care for
8 adolescents. NASPAG supports the availability of
9 oral progesterone-only contraceptive pills to
10 adolescents without a prescription.

11 Mistimed pregnancy occurring during
12 adolescence has lifelong health, social, and
13 economic implications. Oral hormonal contraception
14 has significantly contributed to reducing
15 adolescent pregnancy rates. Providing adolescents
16 with comprehensive reproductive health care during
17 visits with providers is at the core of our
18 mandate, but these conversations should not be
19 barriers to access and contraception.

20 Adolescents face more barriers than adults
21 in accessing comprehensive reproductive healthcare
22 services and abortion care, including cost,

1 confidentiality concerns, and the limited knowledge
2 and experience of the healthcare system.
3 Marginalized teens and those who experience
4 systemic oppression are also uniquely vulnerable.
5 Reducing barriers and ensuring access to
6 contraceptives is a key strategy to prevent
7 unintended teen pregnancies and need for abortions.
8 Youth in many states have limited access to sexual
9 health education and reproductive resources,
10 therefore, over-the-counter access to reliable
11 contraception is particularly essential.

12 Risk of harm related to progesterone-only
13 pills is low and comparable to risks associated
14 with common over-the-counter medications such as
15 acetaminophen, aspirin, and ibuprofen. The need to
16 self-screen for contraindications is simple, and
17 adolescents rarely have medical conditions
18 prohibiting the use of progesterone. A safe
19 over-the-counter birth control option is a timely
20 and important resource to provide equitable access
21 and essential reproductive health care for
22 adolescent patients. Thank you.

1 DR. COYLE: Thank you.

2 We'll move on to speaker number 6. Please
3 unmute and turn on your webcam. Will speaker
4 number 6 begin and introduce yourself? Please
5 state your name and any organization you're
6 representing, for the record.

7 DR. HADDAD: Good afternoon. My name is
8 Lisa Haddad, and I'm an OB/GYN with subspecialty
9 training in complex family planning. I'm here
10 today speaking on behalf of Population Council,
11 where I serve as medical director. Population
12 Council is a nonprofit organization that conducts
13 research and develops new technologies in sexual
14 and reproductive health, including contraceptives.
15 We're committed to developing new methods to meet
16 the needs of people globally.

17 We support the application of Opill for
18 over-the-counter status based both on the science
19 and the clinical results, and recognize the
20 transformational potential of your decision today.
21 I also stand in front of you today speaking from my
22 own personal experience as an OB/GYN practicing in

1 Atlanta, Georgia for over a decade. I have no
2 financial interest in the outcome of this meeting.

3 The data presented at this meeting makes it
4 abundantly clear that a progestin-only pill is an
5 extremely effective product with few
6 contraindications and a simple and clear daily
7 usage pattern. Women, including adolescents, are
8 highly capable to decide to use it and can
9 understand the risks and benefits.

10 I know that your deliberations must consider
11 if an interaction with a medical professional would
12 enhance the delivery of the progestin-only pill.
13 While deep and meaningful interactions with health
14 professionals are often helpful to some patients,
15 these visits are often brief and are not required
16 before a patient starts to use contraception. The
17 decision to use contraception and which type to use
18 is ideally based on the person's preference and
19 values. Medical exams and discussions are not
20 required for a method with the high safety record
21 of the progestin-only pill. Many, if not most, of
22 my patients come in already knowing what they want

1 to use for birth control and are already aware of
2 the risks and benefits. They may not want to hear
3 about alternatives. Their goal is to get something
4 immediately.

5 The barriers to contraceptive access for
6 women based on social economic and bureaucratic
7 factors are real. There are often delays in
8 appointments, difficulty getting insurance
9 approvals, and logistic challenges to access
10 services that we as providers can't control. These
11 barriers can make it impossible for even highly
12 motivated individuals to access care. Therefore,
13 as a provider, I believe that it is in the interest
14 of the health and well-being of my patients to have
15 access to this extremely safe and highly effective
16 method. I should not be the gatekeeper delaying
17 individuals from using this method.

18 I strongly encourage the advisory committee
19 to consider the public health benefit of enabling
20 women to access Opill over the counter. The
21 scientific evidence on safety is compelling. This
22 will not prevent women from having discussions with

1 providers. Your decision can help millions to have
2 easier access to effective contraception. This is
3 important, necessary, and urgent. Thank you for
4 your time.

5 DR. COYLE: Thank you.

6 Speaker number 7, please unmute and turn on
7 your webcam. Will speaker number 7 begin and
8 introduce yourself? Please state your name and any
9 organization you are representing, for the record.

10 MS. YEUNG: Happy Asian Pacific American
11 Heritage Month, everyone. I'm Miriam Yeung. I'm
12 the former executive director of the National Asian
13 Pacific American Women's Forum, and most
14 importantly, the parent of two wonderful teenage
15 girls. I have no disclosures, and I represent
16 myself.

17 Every morning after getting my kids out the
18 door to school -- a minor victory, and some of you
19 know what I'm talking about -- I then open up the
20 paper and read some story of the public health
21 crisis, the reproductive healthcare crisis going
22 on. Abortion is totally banned in 14 states, a

1 6-week ban in one state, and there are 10 cases
2 moving through the courts as we speak. The news
3 changes every day. Texas is home to the third
4 largest Asian American population in the U.S.
5 Georgia, Florida, and Ohio have the fastest growing
6 Asian American populations, and Asian Americans
7 live in each and every one of the states with
8 abortion bans.

9 I read of Jaci Statton, who had a non-viable
10 molar pregnancy, a cancerous pregnancy, and was
11 told to wait in the parking lot of her Oklahoma
12 hospital until her health crashed before they could
13 give her the DNC she needed. I read of Shalon
14 Irving, a brilliant black epidemiologist at the CDC
15 who died 3 weeks after giving birth from
16 complications of high blood pressure, another
17 victim in our maternal mortality crisis.

18 The U.S. is not the best place to be
19 pregnant when you want to have a safe, healthy
20 birth. It's a very hard place to be when you're
21 pregnant and you don't want to be, and it's really
22 not easy to try to stay unpregnant. I have to find

1 a provider; make an appointment; wait; travel
2 there; take time off to see the doctor; get refills
3 on time; et cetera, et cetera. It's even harder if
4 I were an undocumented Asian American working
5 minimum wage and locked out of the Affordable Care
6 Act, or if I were a young person trying to do the
7 right thing without getting in trouble with my
8 parents. I was part of the peer-reviewed paper,
9 where Asian American youth told us that privacy is
10 why they support all contraceptives going over the
11 counter.

12 The most effective contraceptive that people
13 can get at the drug store without a prescription
14 are spermicides and internal condoms, with
15 21 percent failure, or male condoms with 13 percent
16 failure from typical use. Opill is more effective
17 than spermicides, internal condoms, or male
18 condoms. Opill is safer than being pregnant.
19 Opill is safer than Benadryl. If there were a
20 TikTok challenge to take too many Opill, nothing
21 will happen to you but a lesson-inducing hangover.

22 Rarely do we get a chance to effect

1 structural changes, to remove a systemic barrier
2 that drives racial and gender inequity. This
3 advisory committee has that chance. Please vote
4 yes for public health. Please, for the sake of my
5 daughters, vote yes for greater access and
6 autonomy. Thank you.

7 DR. COYLE: Thank you.

8 Speaker number 8, please unmute and turn on
9 your webcam. Will speaker number 8 begin and
10 introduce yourself? Please state your name and any
11 organization that you are representing, for the
12 record.

13 MS. HEIMBROCK: Hello. My name is Rebecca
14 Heimbrock, and I am a rising junior at Whitman
15 College. Thank you for taking the time to listen
16 to my testimony today. People under the age of 18
17 deserve access to safe and effective birth control
18 without stigma. I myself, having grown up in rural
19 Appalachia, have experienced firsthand the stigma
20 that rural medical providers attached to birth
21 control. As a teenager, I was told by my doctor
22 that I shouldn't start the birth control pill

1 because it would make me more likely to become
2 sexually active. Of course, we know that this is
3 not true, and young people without access to birth
4 control simply have sex without being on birth
5 control.

6 In addition, it ignores the fact that birth
7 control pills have other uses, such as making
8 periods more manageable or even chronic pain
9 management for those like me who suffer from
10 endometriosis. For working-class people in rural
11 communities, there is little, if any,
12 infrastructure to support the reproductive health
13 of young people.

14 The COVID-19 pandemic has exacerbated the
15 strain on all healthcare systems, but already
16 underdeveloped systems in rural America are feeling
17 the strain more. Those trying to access critical
18 reproductive health care are stymied by a lack of
19 providers, a lack of transportation, and high
20 costs. My Appalachian community only had one local
21 health clinic, and their services were severely
22 limited. For any healthcare needs that couldn't be

1 addressed by the clinic, we had to drive an hour
2 outside of town to the nearest medical center. How
3 our young people in rural communities supposed to
4 access something as simple as the birth control
5 pill if, like me, they are unable to have even
6 their most basic needs met by their local
7 healthcare providers?

8 It is no surprise, then, that rural teens
9 are more likely to experience teen pregnancy and
10 report higher barriers to accessing birth control.
11 If Opill were available over the counter, rural
12 youth could access this life-changing care online
13 with ease, reducing unintended pregnancies and
14 changing the course of their lives.

15 Throughout the course of the COVID-19 health
16 crisis, the CDC has told us time and again to
17 follow the science. I'm here to tell the FDA the
18 same. Follow the science, and to make Opill
19 available over the counter for all ages. The
20 critical lack of reproductive health care in rural
21 and working-class communities is a health crisis.
22 If the FDA makes this switch, it would make that

1 crisis just a little better and change the lives of
2 rural young people across the country. Thank you.

3 DR. COYLE: Thank you.

4 Speaker number 9, please unmute and turn on
5 your webcam. Will speaker number 9 begin and
6 introduce yourself by stating your name and any
7 organization that you are representing, for the
8 record?

9 MS. MANSON: Good afternoon. I'm Jamie
10 Manson, president of Catholics for Choice. I have
11 a Master of Divinity degree from Yale in Catholic
12 theology and medical ethics, and I did my research
13 under one of the country's leading Catholic medical
14 ethicists, Sister Margaret Farley. Catholics for
15 Choice has no financial conflicts of interest.

16 I'm here today to state unequivocally that
17 Catholics overwhelmingly support the use of birth
18 control. Indeed, even though the hierarchy of the
19 Catholic church continues to condemn the use of
20 artificial contraception, 89 percent of lay
21 Catholics believe that contraception is either
22 morally acceptable or not a moral issue at all, and

1 98 percent of sexually active Catholic women have
2 used contraception.

3 I'm focusing on the Catholic church's
4 teaching today because the church is one of the
5 original primary sources of stigma, shame and,
6 indeed, misinformation about birth control pills.
7 The church's all male, celibate hierarchy
8 officially banned all forms of artificial
9 contraception less than 100 years ago, and this
10 teaching has had undue influence on U.S. healthcare
11 policy since, and one could argue now more than
12 ever.

13 The powerful truth is there is much in
14 Catholic teaching that could bless the idea of OTC
15 birth control. For example, a fundamental Catholic
16 teaching is that a person's individual conscience
17 must be the final arbiter in all moral decision
18 making, even if it contradicts the church's
19 official position. Over-the-counter access to
20 birth control pills advances this kind of moral
21 autonomy.

22 The church also teaches the notion of

1 responsible parenthood, saying that it's a moral
2 duty for couples to determine the number, spacing,
3 and timing of their children, taking into account
4 their own physical, economic, psychological, and
5 social conditions, as well as their ability to
6 provide for the health, education, and growth of
7 their children. Offering birth control over the
8 counter ensures that families will have the
9 resources necessary to follow through on those
10 decisions.

11 The church's rich social tradition calls us
12 to have a special concern for society's most
13 vulnerable, particularly those struggling with
14 economic insecurity, those facing violence, like
15 violence at home, those living in rural areas, and
16 immigrants. OTC access to birth control pills will
17 reduce many barriers to contraception and advance
18 health care, especially for those most in need.

19 Sadly, for years, some Catholic leaders have
20 advanced the argument that birth control pills can
21 induce abortion. This claim is false, lacks any
22 scientific or medical backing, and has even been

1 debunked by the official Journal of the Catholic
2 Health Association. Regardless of what Catholics
3 believe, freedom of religion should include the
4 right to be free from the religious beliefs of
5 others. No religious group should block the
6 accessibility of any FDA-approved medication.

7 Decades of use and research demonstrate that
8 birth control pills are safe and highly effective
9 at preventing pregnancy and meet the FDA's criteria
10 to be available without a prescription. As a
11 Catholic leader, I implore you to vote yes to bring
12 Opill over the counter. Thank you.

13 DR. COYLE: Thank you.

14 We'll move on to speaker number 10. Speaker
15 number 10, please unmute and turn on your webcam.
16 You may begin and introduce yourself by stating
17 your name and any organization that you are
18 representing, for the record.

19 MS. RENKO: Good afternoon. My name is
20 Caroline Dezai [ph] Renko, and I am the project
21 manager at PharmedOut, a rational prescribing
22 project at Georgetown University Medical Center,

1 and I have no conflicts of interest. Today we urge
2 the FDA to approve Opill as the first over-the-
3 counter oral contraceptive in the United States.
4 The fight for access to effective nonprescription
5 women-controlled contraception has been ongoing for
6 more than half a century. Oral contraceptives are
7 available over the counter in many other countries,
8 and it's about time that the United States caught
9 up.

10 Since the approval of the first prescription
11 birth control pill in 1960, numerous studies have
12 shown oral contraception to be both safe and
13 effective. Opill has been on the market since 1973
14 and has an excellent safety record. Other
15 over-the-counter medications, including aspirin,
16 ibuprofen, and Tylenol, are far more dangerous.

17 Over-the-counter medications are supposed to
18 be safe and effective when used as directed for
19 self-diagnosed conditions. No condition is easier
20 to self-diagnose than being at risk of pregnancy.
21 Today the birth control pill is the most commonly
22 prescribed form of contraception, but there is

1 still a glaring issue of access, especially for
2 adolescents and young women. There are so many
3 barriers, including lack of parental support, lack
4 of access to health care, the cost associated with
5 a doctor's visit, among others.

6 In 2021, 1 in 10 women in the United States
7 reported having no personal healthcare provider.
8 Women of color were least likely to have access.
9 Over-the-counter contraception eliminates this
10 hurdle for disadvantaged women. Although
11 medication costs could still be a barrier for some,
12 approving Opill is a step in the right direction.

13 In some states, women can still be denied
14 birth control pills by a pharmacist, citing moral
15 or religious obligations. Religious beliefs should
16 not straightforwardly fix this by making oral
17 contraception available over the counter. We have
18 heard concerns that women who don't take Opill at
19 the same time every day could experience unintended
20 pregnancies. These concerns apply equally to
21 low-dose combined oral contraceptives. Women can
22 understand labels, including contraindications. In

1 addition, birth control pills are so commonly used
2 that information regarding the importance of not
3 missing doses or taking doses late is common
4 knowledge. In any case, these patronizing concerns
5 are not grounds to take away a woman's choice from
6 her.

7 At a time when abortion rights are being
8 stripped away state by state, equitable access to
9 effective birth control is critical to women's
10 reproductive freedom. In light of Roe v. Wade
11 being overturned and growing state restrictions on
12 abortion, there has never been a greater need for
13 increased access for women-controlled effective
14 birth control. Women's health activists have been
15 fighting for over-the-counter birth control pills
16 from before I was born. I hope to be a part of the
17 generation that benefits from my foremothers'
18 fight. Thank you very much.

19 DR. COYLE: Thank you.

20 We will move on to speaker number 11.
21 Please unmute and turn on your webcam. Will
22 speaker number 11 begin and introduce yourself by

1 stating your name and any organization you are
2 representing, for the record?

3 MS. BLANCHARD: Thank you, and good
4 afternoon. My name is Kelly Blanchard. I'm the
5 president of Ibis Reproductive Health. My
6 colleagues at Ibis and I have been involved in
7 research and coalition efforts to make an oral
8 contraceptive over the counter for two decades, and
9 that work has helped us get to this historic Free
10 the Pill Day.

11 The data is clear that progestin-only pills
12 are extremely safe and effective and appropriate
13 for people of all ages. Norgestrel was approved
14 50 years ago, and progestin-only pills have been
15 safely used by millions of people for decades. As
16 noted earlier today, an over-the-counter
17 progestin-only pill would mean people have access
18 to an OTC method that is much more effective than
19 current OTC methods. Our research has shown that
20 people are supportive of an over-the-counter
21 progestin-only pill and interested in using an
22 over-the-counter progestin-only pill. Importantly,

1 we have found that people who are not currently
2 using a method are interested in this option.

3 I also want to make sure everyone on this
4 committee was aware of the Border Contraceptive
5 Access study, showing that people who had access to
6 their birth control pills over the counter were
7 more likely to continue use, showing how
8 over-the-counter access helps overcome barriers and
9 could lead to higher use effectiveness. Findings
10 from that study also showed that people accessing
11 birth control pills over the counter got
12 recommended preventive screening at higher levels
13 than in the general population.

14 Although there's not enough time to address
15 many of the points laid out in the FDA's
16 presentation today, as an expert on contraception,
17 I do not share concerns about efficacy of Opill in
18 an over-the-counter environment and am surprised
19 they did not consider the possibility of higher
20 effectiveness in OTC settings, given the published
21 literature.

22 Our research at Ibis also highlights how

1 this switch is important for public health and
2 health equity. Nearly one-third of women who have
3 ever tried to get a prescription for birth control
4 or refill it have faced barriers. In research
5 focusing on black, indigenous, Latinx, Asian
6 American, Pacific Islander, and other folks of
7 color, that figure is even higher. Forty-five
8 percent faced a barrier accessing a prescription
9 method. In that study, 71 percent of people of
10 color who weren't currently using any contraceptive
11 method reported they would be likely to use an
12 over-the-counter birth control pill.

13 All of us, including young people, should
14 have access to the contraception we need without
15 unnecessary barriers so we can make decisions about
16 our health, our futures, and our families. An
17 over-the-counter pill that's affordable, fully
18 covered by insurance, and available to people of
19 all ages will be an important advance and help
20 people who need and want birth control, and it will
21 help them to get it without barriers.

22 The FDA should follow the science, including

1 the robust data on Opill's safety and effectiveness
2 and the data on the important public health and
3 health equity benefits of an over-the-counter birth
4 control pill when considering this application.

5 Thank you for your time.

6 DR. COYLE: Thank you.

7 We will move on to speaker number 12.

8 Please unmute and turn on your webcam. Will
9 speaker number 12 begin and introduce yourself?

10 Please state your name and any organization you are
11 representing, for the record.

12 MS. MASKE: Good afternoon. My name is
13 Angela Maske, and I am with Advocates for Youth and
14 co-author of the 2022 Oral Contraceptives Access
15 Survey, Behind the Counter. As an advocate who
16 works directly with young people, I am in strong
17 support of over-the-counter approval of Opill with
18 no age restriction.

19 For this report, we surveyed 243 individuals
20 recounting experiences from ages 13 to 25.

21 Eighty-eight percent of respondents reported
22 experiencing at least one barrier to accessing oral

1 contraception as a young person; 55 percent
2 reported that the barriers they experienced
3 prevented them from accessing oral contraception
4 altogether. Of that 55 percent, 58 percent had a
5 pregnancy scare and 20 percent experienced an
6 unintended pregnancy.

7 The barriers that young people in particular
8 are facing are so serious that for many, it is
9 preventing them from getting on birth control pills
10 when they would want to be or interrupting their
11 usage of the pill, and the impacts of these
12 barriers are serious, too. Respondents have
13 reported not only unintended pregnancies, but
14 health complications, financial problems, and
15 emotional and psychological stress and trauma
16 resulting from the consequences of their lack of
17 access to oral contraceptives.

18 This issue isn't just about numbers. It's
19 about the very real difficulties, challenges, and
20 pain that young people experience under the
21 prescription-only system. I would like to
22 highlight some of these experiences collected

1 through our survey today.

2 "My lack of birth control access resulted in
3 me getting pregnant and then miscarrying. This has
4 affected my mental health a lot, and I will never
5 be the same person I was before. Birth control
6 should be much more accessible for everyone." From
7 Madalyn in North Dakota.

8 "I needed my parents to use our insurance
9 and bring me to the doctor, but I didn't want my
10 parents to get angry with me for having sex, and
11 lying to them about why I needed birth control was
12 hard for me. So I didn't get on birth control when
13 I wanted to. I wanted to have safe sex, but there
14 were so many barriers and it made things
15 difficult." From Anna in Minnesota.

16 "I'm from a military family and have moved
17 four times in the last five years. The
18 prescription requirement made it extremely
19 difficult to refill my birth control each time I
20 moved because the official transfer of paperwork
21 often took several weeks. This in turn caused me
22 to miss several pills and therefore have to deal

1 with the adverse side effects of this disruption."

2 From Meghan in Colorado.

3 "As a teenager, I wanted to go on birth
4 control, but my doctor was extremely judgmental,
5 going so far as to tell me teenage girls don't like
6 sex. Then I tried to go to Planned Parenthood, but
7 I was afraid my parents would find out. So I used
8 condoms, but I had several very stressful pregnancy
9 scares between the ages of 15 and 19." Elizabeth
10 in New Jersey.

11 The story shared by young people in our
12 report clearly show that access barriers affect
13 individuals in numerous ways across a variety of
14 life's circumstances, and most severely when they
15 are under 18. I strongly urge the advisory
16 committee to vote yes to approving Opill as an
17 over-the-counter oral contraceptive option without
18 an age restriction. Thank you.

19 DR. COYLE: Thank you.

20 We'll begin with speaker number 13. Please
21 unmute and turn on your webcam. Will speaker
22 number 13 begin and introduce yourself by stating

1 your name and any organization you are
2 representing, for the record?

3 DR. GROSSMAN: Good afternoon, and thank you
4 for the opportunity to speak. My name is Daniel
5 Grossman, and I'm a professor of obstetrics,
6 gynecology, and reproductive sciences at the
7 University of California San Francisco, and I have
8 no financial relationships to disclose.

9 Between 2005 and 2011, I was a
10 co-investigator on the Border Contraceptive Access
11 Study led by Joe Potter at the University of Texas
12 in Austin, which was funded by the National
13 Institute of Child Health and Human Development.
14 During that project and in subsequent research, I
15 led or co-led several studies related to
16 over-the-counter access to oral contraceptives, and
17 I'd like to highlight some of that research to make
18 the point that there is substantial evidence beyond
19 the specific studies performed by HRA Pharma that
20 indicates that oral contraceptives, and
21 particularly a progestin-only formulation, are
22 appropriate for nonprescription status.

1 First, our research has consistently
2 demonstrated that there is considerable demand for
3 OTC oral contraceptives, particularly among people
4 who currently face barriers accessing effective
5 contraception. Often this interest, as we've heard
6 recently in some of the other testimony, is because
7 people feel that removing the prescription
8 requirement would improve access to this effective
9 method, making it more convenient both to initiate
10 and to continue to use oral contraceptives, thereby
11 helping to reduce gaps in use.

12 Our research also explored contraindications
13 to oral contraceptives and found that potential
14 users were quite accurate in self-selecting or
15 self-screening for these conditions. In
16 particular, contraindications to progestin-only
17 oral contraceptives are rare, occurring in less
18 than 1 percent of people of reproductive age, and
19 potential users can accurately identify these
20 conditions on their own without a learned
21 intermediary since the screening is based on
22 medical history alone. A history of breast cancer,

1 the only absolute contraindication, occurs in about
2 half a percent or less of people in this age
3 category, and my research found that people were
4 able to accurately identify this history on their
5 own and were able to appropriately self-select.

6 In the Border Contraceptive Access Study, we
7 compared several outcomes between women living in
8 El Paso, Texas, who obtained oral contraceptives in
9 clinics in Texas, to a group living in El Paso who
10 obtained oral contraceptives over-the-counter in
11 Mexican pharmacies. We found that discontinuation
12 of oral contraceptives was significantly higher for
13 those obtaining the method in clinics on
14 prescription, indicating an advantage for the OTC
15 users. In another study from this project, we
16 found that preventive screening for cervical cancer
17 and sexually transmitted infections was very high
18 among people obtaining OTC oral contraceptives in
19 Mexico and above the national U.S. average.

20 I believe that the research strongly
21 supports approval of this norgestrel product for
22 nonprescription status for users of all ages.

1 There's no reason to exclude young people who face
2 more barriers to effective contraception from this
3 expanded model of access. I urge the committee to
4 consider the large body of evidence pointing to a
5 public health benefit from over-the-counter access
6 to oral contraceptives. Thank you.

7 DR. COYLE: Speaker number 14, please unmute
8 and turn on your webcam. Speaker number 14, you
9 may begin and introduce yourself by stating your
10 name and any organization you are representing, for
11 the record.

12 MS. NELSON: Thank you. Good afternoon,
13 members of this esteemed committee. My name is Bo
14 Nelson. I'm a newly 20-year-old college student
15 advocating for the advisory committee to follow the
16 science and consider the life changing impact that
17 a safe, affordable, over-the-counter birth control
18 option with no age restriction can make for people
19 across the United States.

20 Access to birth control has been something
21 that has impacted my life, the lives of so many of
22 my friends, and the lives of people around me

1 who've told me their stories or who I've directly
2 supported no matter how I met them. It's
3 intimately tied with my life. And now more than
4 ever, bodily autonomy and the right to prevent and
5 decide when and if one gets pregnant is one that we
6 face so many barriers to, especially after the
7 overturn of Roe v. Wade and the very real barriers
8 the prescription-only model poses to all, but
9 especially the most vulnerable.

10 When I was 12 years old, I got my first
11 period. My mother brought me to the gynecologist
12 when she noticed I was having periods so heavy they
13 made it difficult to go to school when I was on my
14 period. We knew that birth control could be used
15 to manage light and even skip periods, but when I
16 came to doctors, they were uncomfortable with
17 giving a 13 year old birth control. Why? The
18 stigma of young people having sex.

19 It took three doctors visits to finally find
20 a non-judgmental nurse practitioner by the time I
21 was 14. Birth control completely changed my life.
22 It managed by heavy periods, it let me finish high

1 school without the stress of teen pregnancy, and
2 now in college, it's allowing me to achieve my
3 career goals of becoming a reproductive health
4 provider who's currently an undergrad.

5 Later when I was in high school, I became a
6 peer sex educator, where I learned that at the
7 local health department, teens could get birth
8 control for free without needing to notify their
9 parents; however, this was only if they could prove
10 they were under 18, they had their social security
11 number, and the health department was a 45-minute
12 drive away: age, driver's license, a car, and
13 privacy if you needed it; lots of barriers here.

14 As a peer educator, I started driving my
15 friends and people I barely knew multiple times a
16 month. Some people's parents knew and totally
17 supported them, and they just couldn't take time
18 off work to access this cheaper birth control.
19 Others had parents where a conversation about birth
20 control and sex were out of the question. For
21 people of all ages, so many barriers exist, and
22 it's a complex, individual, personal decision.

1 Now, I'm in Western Massachusetts at
2 Williams College. Because I'm going to a rural,
3 out-of-state school, and my gynecologist is in
4 Florida wanting an in-person visit before they'll
5 refill my birth control prescription, I don't have
6 consistent birth control right now. Shouldn't
7 simply not wanting to be pregnant and feeling birth
8 control is the right choice for myself not be
9 enough?

10 Williamstown is a reproductive health
11 desert, and over 19 million women live in
12 contraceptive deserts nationwide. There's a
13 9-month wait list for IUDs at our overwhelmed local
14 hospital. The closest Planned Parenthood is an
15 hour away, and freshman on our campus aren't
16 allowed to have their own vehicles if they have a
17 license or car at all.

18 I hope you see through my experience the
19 range of barriers one person will face in one
20 lifetime and how simply being able to pick up birth
21 control pills at CVS or Walgreens without all the
22 gatekeeping would be transformative. These barriers

1 represent only a few, and those on the margins
2 experience the most barriers in terms of
3 criminalization, stigma, and access and cost
4 challenges under the current system, and we need to
5 recognize that. I urge the committee to allow for
6 this over-the-counter birth control option with no
7 age restrictions. Thank you.

8 DR. COYLE: Thank you.

9 Speaker number 15, please unmute and turn on
10 your webcam. You may begin and introduce yourself
11 by stating your name and any organization you are
12 representing, for the record.

13 MS. SRINIVASAN: Good afternoon, esteemed
14 members of the FDA advisory committee. My name is
15 Sriha Srinivasan, and I'm here today to advocate
16 for over-the-counter access to the birth control
17 pill for all ages. I have no financial
18 stipulations to disclose.

19 While I speak on behalf of myself, I have
20 seen firsthand the impact that lack of access to
21 contraception can and does have on young people. I
22 created @sexedu while I was in high school, a

1 platform on social media where I destigmatize
2 sexual health through short-form sex education
3 content. My videos have been shared with and
4 interacted with by millions of Americans, with over
5 80 percent of my audience being under the age of
6 25. Through numerous conversations on this
7 platform over the years surrounding contraception,
8 I have found that young Americans lack access to
9 birth control due to barriers between them and
10 accessible impartial care.

11 SisterSong defines reproductive justice as a
12 human right to maintain personal bodily autonomy,
13 have children, not have children, and parent the
14 children we have in safe and sustainable
15 communities. The barriers between Americans and
16 birth control degrade this human right, as it
17 pertains to personal bodily autonomy and the right
18 to not have children.

19 Allow me to walk through one of the
20 countless examples I have gathered during my time
21 as a sexpert at UCLA, where I am graduating this
22 year with a BS in human biology and society. A

1 student joining my university in the fall would
2 like to get on birth control. The first step is
3 insurance. Can they afford the \$741.90 it cost per
4 quarter for university health care or do they have
5 their own? If they have their own, where is the
6 nearest provider accepting new patients?

7 Students report having to schedule
8 appointments out for months in advance through both
9 the university and private practice without knowing
10 if their class or work schedules will still be
11 accommodating, or if the provider they're seeing
12 will even be supportive of their intention to get
13 on birth control.

14 Then there's the matter of getting to said
15 appointment. Even in Los Angeles, one of the
16 biggest metropolitan hubs of the country, students
17 share experiences of having to navigate complicated
18 public transportation, spending hours and making
19 multiple transfers to get to and from a doctor's
20 office. And on top of it all, there's the cost of
21 the visit, especially if one's family is not
22 inclined to pay for access to contraception. This

1 example is comprehensive, and each of these
2 questions is far from rhetorical. They represent
3 real tangible barriers my peers and myself face
4 every single day.

5 While mountains for my college classmates,
6 these barriers are even more significant for high
7 school students. As a high school freshman, my
8 younger sister can walk into a retail pharmacy,
9 pick up Tylenol for a cold, and be trusted to
10 self-diagnose, self-manage, and self-treat her
11 symptoms.

12 The FDA already trusts young people to buy
13 Plan B or emergency contraception over the counter,
14 and the same allowance should be afforded to the
15 birth control pill; yet for my sister to access her
16 human right to maintain personal bodily autonomy
17 and not have children through oral contraception,
18 she must face barriers upon barriers that can be
19 failed down in one swoop by the FDA.

20 As a young person, advocate, and future
21 healthcare provider, I implore you today to
22 consider the urgent need for over-the-counter

1 access to birth control as an option young people
2 of all ages can choose in the United States, and
3 vote yes in your consideration. Thank you for your
4 time.

5 DR. COYLE: Thank you.

6 Speaker number 16, please unmute and turn on
7 your webcam. Will speaker number 16 begin and
8 introduce yourself? Please state your name and any
9 organization you are representing, for the record.

10 DR. UPADHYA: Good afternoon. My name is
11 Krishna Upadhy, and I have dedicated my career to
12 ensuring access to sexual and reproductive health
13 care as a clinician, researcher, educator, and
14 advocate. As a board-certified adolescent medicine
15 specialist and pediatrician, I've delivered care to
16 young people in various settings, including Title X
17 funded clinics, school-based health centers, and
18 hospitals. I'm also a clinician scientist and have
19 published extensive research on the topic of
20 adolescent medicine. I do not have any financial
21 disclosures to make.

22 Today, I provide testimony on behalf of

1 Planned Parenthood Federation of America, where I
2 currently serve as vice president of quality care
3 and health equity. Planned Parenthood is the
4 nation's leading provider and advocate of
5 high-quality affordable sexual and reproductive
6 health care for all people.

7 Planned Parenthood strongly supports over-
8 the-counter availability of Opill because the
9 medication is safe and effective. OTC availability
10 would help to bridge gaps in access for people who
11 face the most barriers to prescription-only
12 contraception, and OTC availability would provide
13 another needed contraceptive option for people who
14 do not want to be pregnant, especially for those
15 living in states that ban or restrict abortion.

16 I want to speak today about the crucial need
17 for Opill to be made available OTC to people of all
18 ages who need pregnancy prevention. In my career,
19 I have cared for many young people facing
20 unexpected pregnancy and those seeking
21 contraception. Our review of existing scientific
22 evidence I published with other adolescent

1 healthcare experts confirms that oral
2 contraceptives are safe and effective for
3 adolescents, and there is no scientific rationale
4 for limiting OTC access by age. Contraindications
5 to any oral contraceptive are very uncommon among
6 adolescents, and Opill has almost none of those
7 contraindications.

8 In addition, adolescents, as I think the
9 young people on this call have demonstrated today,
10 are very capable. They can self-screen for
11 contraindications to oral contraceptives. My
12 research also indicates that adolescents are able
13 to use oral contraceptives correctly and with low
14 contraceptive failure rates. This research is
15 cited in my written testimony submitted to the
16 committee.

17 OTC contraceptive access is vital for young
18 people because they face multiple and intersecting
19 barriers to obtaining prescription-only
20 contraception. Adolescents may feel uncomfortable
21 or unsafe asking their parents for help getting
22 prescription for contraception or their parents may

1 prevent them from accessing contraception. A young
2 person may be unable to independently travel to a
3 healthcare provider, take time off from school, or
4 afford the cost of an appointment. In addition,
5 young people may avoid using their insurance to
6 maintain confidentiality, magnifying these
7 financial barriers.

8 Planned Parenthood strongly advocates for
9 the committees to follow the robust body of
10 scientific evidence, demonstrating that adolescents
11 and all people can use Opill over the counter.
12 Young people should have the tools and resources
13 they need to plan their futures. Thank you for the
14 opportunity to testify today.

15 DR. COYLE: Speaker number 17, please unmute
16 and turn on your webcam. Will speaker number 17
17 begin and introduce yourself by stating your name
18 and any organization you are representing, for the
19 record?

20 MS. WATKINS: Good afternoon, members of
21 the advisory committee. My name is Robin Watkins,
22 and I'm the senior director of health care at Power

1 to Decide. I have no conflicts of interest to
2 disclose. I am also a certified nurse midwife and
3 women's health nurse practitioner, providing sexual
4 and reproductive health care here in the
5 Washington, DC area. Power to Decide is a
6 nonprofit, non-partisan organization that works to
7 advance sexual and reproductive well-being for all.

8 Power to Decide strongly endorses the
9 approval of Opill for over-the-counter
10 nonprescription use without an age restriction,
11 based on the strong evidence of safety and
12 efficacy, the impact an OTC pill can have on
13 addressing inequitable access to birth control
14 pills, and the broad support for this move.

15 Research from Power to Decide shows that
16 more than 19 million women of reproductive age in
17 need of publicly funded family planning live in
18 contraceptive deserts, counties where they lack
19 reasonable access to a health center offering the
20 full range of contraceptive methods. We also know
21 that those living in contraceptive deserts are more
22 likely to be people of color and those living in

1 rural communities.

2 When you live in a contraceptive desert, you
3 need to travel further to get your birth control
4 from a healthcare provider, and just to get to your
5 appointment, you'll need to take more time off work
6 or arrange more childcare. However, counties
7 considered to be contraceptive deserts typically
8 have pharmacies or other retail settings where an
9 OTC birth control pill could be available. For
10 individuals living in those communities, this
11 option could substantially improve their access to
12 birth control pills. An OTC birth control pill
13 approved without age restrictions could also help
14 address unique access barriers that young people
15 face such as concerns about lack of confidentiality
16 when going to a health center.

17 Research demonstrates that young people have
18 the capacity to follow package instructions to use
19 OTC birth control pills safely and effectively. It
20 should be noted that age restriction can also
21 impact adults who lack government identification,
22 who are disproportionately people of color.

1 Research shows people want an OTC birth control
2 pill. More than three-quarters of people surveyed
3 across the country favor making birth control pills
4 available over the counter without an age
5 restriction. Additionally, studies showed that
6 people of all ages, including young people, will
7 still see their healthcare provider for needed care
8 even when getting their birth control pills OTC.

9 In addition to broad support from
10 contraceptive users themselves, it's worth noting
11 the broad support for OTC birth control pills from
12 healthcare providers like myself and the
13 professional organizations that represent them,
14 many of whom are speaking here today in support of
15 over-the-counter access. On behalf of Power to
16 Decide, I urge the advisory committee to consider
17 both the strong evidence of safety and efficacy, as
18 well as the significant need for an
19 over-the-counter pill at a time when too many
20 people struggle to access birth control. Thank you
21 for your time.

22 DR. COYLE: We'll move on to speaker

1 number 18. Please unmute and turn on your webcam.
2 Speaker number 18, you may begin and introduce
3 yourself by stating your name and any organization
4 you are representing, for the record.

5 MS. MUSKETT: I'm Susan Muskett, president
6 of Pro-Family Women, and we oppose this proposal to
7 allow over-the-counter access to the Opill
8 contraceptive pill. Our longer comments were
9 posted by the FDA on regulations.gov. We have no
10 financial relationships.

11 A key issue is whether the FDA will allow
12 minor girls over-the-counter access to Opill
13 without their parents' permission. If an
14 adolescent has not used birth control, it would
15 mean that their first exposure to birth control,
16 with all its potential side effects and strict
17 criteria for proper use to avoid pregnancy, would
18 be by picking up a package of pills off the store
19 shelf. Vigilance in following the manufacturer's
20 instructions is especially important with regard to
21 Opill, as it must be taken at the same time each
22 day.

1 Parents should always be involved in their
2 minor daughter's medical care and medication so
3 that they can watch her side effects. Research has
4 shown that one of the most serious risks associated
5 with a progestin-only contraceptive for adolescent
6 girls is depression and attempted suicide. Some
7 people may argue the benefit of preventing teen
8 pregnancy outweighs the risk of side effects, but
9 Professor Helen Alvare, a preeminent scholar of
10 family law, has noted that there is, quote, "a body
11 of research showing that while declines in teen
12 pregnancy may occur after contraception is rendered
13 more accessible to teens who are already sexually
14 active but not using it, with respect to teens who
15 are not sexually active, increased access to
16 contraception is associated with the normalization
17 of non-marital sex and an increase in teen sexual
18 behavior, leading to more teen pregnancies and
19 abortions overall."

20 It is particularly in the area of sexuality
21 that parental involvement must be respected.
22 Facilitating sexual promiscuity by minors through

1 access to contraception is in direct opposition to
2 the belief of Christians and many other people of
3 faith that sexual relations are reserved for
4 marriage.

5 It is estimated that only 4 percent of
6 American women using an oral contraceptive pill use
7 a progestin-only pill. It is hard to imagine any
8 set of documents and protocols that could replace
9 sitting down with a medical provider to learn about
10 the side effects and contraindications of drugs
11 that a woman may be on for decades. The FDA
12 briefing document itself warns of a potential risk
13 for women if they have a history of breast cancer,
14 experience vaginal bleeding, or use other
15 medications that could affect the efficacy of the
16 Opill in preventing pregnancy.

17 Today's women are constantly inundated with
18 fine print. Without the benefit of having seen a
19 healthcare provider, how many women and girls are
20 going to know that they must use a backup
21 contraceptive if they are late in taking the pill
22 that day, or if they vomit within 4 hours of taking

1 the pill that day? Will she know that St. John's
2 wort can reduce the effectiveness of Opill in
3 preventing pregnancy?

4 Close to half of women who experience
5 unintended pregnancy are already using
6 contraception during the month that they become
7 pregnant. Clearly, American women's use of
8 contraceptives when put into real-world practice
9 often do not prevent pregnancy. We urge you to
10 oppose this application. Thank you.

11 DR. COYLE: Speaker number 19, please unmute
12 and turn on your webcam. You may begin and
13 introduce yourself by stating your name and any
14 organization you are representing, for the record.

15 DR. WANG: Hi. My name is Dr. Lin-Fan Wang.
16 My pronouns are she and hers. I am here as a
17 family physician and a complex family planning
18 specialist to submit public comment in favor of the
19 OTC Opill application before the FDA. I have no
20 financial disclosures. I am affiliated with a
21 medical-legal collective, Circle of P [ph], a
22 family physicians of color collective center's

1 health, and QueerDoc, an LGBTQ+ telemedicine
2 company.

3 I am here on behalf of my patients and the
4 communities I serve because access to contraception
5 is already too difficult for too many people. I
6 practice in a variety of clinics throughout
7 Pennsylvania and New York, as well as telemedicine
8 clinics in multiple states, providing care for
9 people of all ages and genders. I prescribe
10 contraceptive pills to prevent pregnancy, to manage
11 menstrual symptoms, and to suppress menstruation.

12 I was denied contraception by my family
13 physician, who knew that I was a physician, who
14 specializes in reproductive health care. He said
15 that I was required to see an OB/GYN for an annual
16 exam before he prescribed the contraceptive method
17 that I had been taking for years. I had the
18 medical knowledge to know that a pelvic exam, or
19 any exam, is not medically necessary before
20 starting or continuing contraception. If this
21 happened to me, then this means that this is not a
22 rare occurrence and impacts people who do not have

1 the education or the power that I do when
2 navigating health care.

3 Throughout my career, I have had many
4 patients who had unwanted pregnancies because they
5 lacked access to their contraceptive method. When
6 considering the studies presented today, it is
7 important to consider that for many, their only
8 alternative is a lower efficacy method or no method
9 at all. Barriers to prescriptions have a greater
10 impact on people from marginalized communities,
11 including people of color, immigrants, adolescents,
12 people living with disabilities, rural residents,
13 and people with low literacy.

14 Transgender and gender non-binary people
15 also use contraception, but they are much less
16 likely to access health care due to fear of or
17 actual experiences with discrimination, stigma, or
18 violence when traveling to a clinic or directly
19 from their healthcare provider, or they are
20 outright denied health care.

21 Based on the science, my medical
22 professional organization, the American Academy of

1 Family Physicians, supports OTC contraception. My
2 experience as a family physician and a complex
3 family planning specialist has shown me that people
4 are savvy. My patients know how to make their own
5 risk assessment about their health and their lives,
6 and the people who seek OTC contraception are no
7 different. It is a public health imperative to
8 make contraceptive pills as easy as possible to
9 access. I encourage the FDA advisory committee to
10 vote yes to making the Opill OTC. Thank you for
11 your time.

12 DR. COYLE: Speaker number 20, please unmute
13 and turn on your webcam. Will speaker number 20
14 begin and introduce yourself? Please state your
15 name and any organization you are representing, for
16 the record?

17 MS. BLANCO: Hello. My name is Jacqueline
18 Blanco. I have no disclosures, and I represent
19 myself. I'm a nurse, and I'm a clinical nurse
20 leader at a public district hospital. I'm an
21 active member of the Association of Women's Health,
22 Obstetrics, and Neonatal Nurses, the governing body

1 of my profession. I'm also a person with a uterus,
2 who cares for many people with uteruses.

3 I grew up in Washington State, and I am not
4 only grateful but proud to be from a state where
5 abortion is legal and protected, but my rights are
6 not set in stone, and access remains tenuous.

7 Abortion is near impossible in 15 states, with more
8 cases passing through the courts now. The influx
9 of patients from states with restricted access
10 grows every day. Higher out-of-state patient
11 volumes are forcing delays not just in abortion
12 services, but in all types of care. We are already
13 facing a nursing shortage. Lack of access to
14 comprehensive reproductive care is exacerbating it.

15 Last month, I organized care for a patient
16 with fetal anomalies that were incompatible with
17 life and complications of pregnancy, constituting a
18 high level of maternal mortality. To say this more
19 clearly, this baby could not live, and likely the
20 mother would not live without intervention. Grief
21 stricken, our patient made the choice to proceed
22 with terminating the pregnancy and inducing labor,

1 but there was a barrier. We could not find her an
2 appointment for over 8 days.

3 We are overwhelmed with patients that had
4 more acute need for treatment. This patient was
5 expected to wait until her baby died spontaneously
6 or her condition worsened to the extent that she
7 would be deemed sick enough to receive the medical
8 care that she already required.

9 Delays of care require nurse leaders like
10 myself to develop strategies to allocate care and
11 triage our patients, strategies that are homegrown
12 and formed with the best intent, but rife with
13 inconsistencies and very prone to inequity. This
14 is in a state with expanded access to reproductive
15 care where abortion is protected.

16 Our patient received care. She lived, but
17 many others won't. Pregnant and postpartum people
18 in the U.S. are dying. It was safer for my mom to
19 have a baby than for me to. BIPOC people like me
20 bear the burden of the mortality crisis, being
21 2 to 3 times more likely to die than white peers,
22 with upwards of 80 percent of those deaths deemed

1 preventable.

2 To avoid maternal deaths, the World Health
3 Organization declared it is vital to prevent
4 unintended pregnancies. Preventing unintended
5 pregnancies is the primary recommendation of our
6 global leaders in evidence-based health promotion,
7 and we have failed. Right now, the most available
8 contraceptives include condoms, sponges, and
9 spermicides. These methods have anywhere from a
10 13 to 20 percent failure rate with typical use, and
11 this is insufficient. Opill is safe and effective
12 in preventing unintended pregnancies. Opill will
13 not only save lives but will keep our healthcare
14 system from collapsing.

15 The advisory committee has the opportunity
16 to change their trajectory of public health across
17 our nations. Nurses support saying yes, AWHONN
18 supports saying yes, the communities I serve
19 support saying yes to oral over-the-counter
20 contraceptives. Please hear my testimony, and vote
21 yes. Also, Happy Nurses Week.

22 DR. COYLE: Speaker number 21, please unmute

1 and turn on your webcam. You may begin and
2 introduce yourself by stating your name and any
3 organization you are representing for the record.

4 DR. PERRITT: Hello. Good afternoon,
5 everyone. My name is Dr. Jamila Perritt, and I am
6 the president and CEO of Physicians for
7 Reproductive Health, a network of doctors across
8 the country, working to advance access to
9 comprehensive reproductive health care, including
10 contraceptive care for all people. I have no
11 financial ties to industry to disclose.

12 I'm a board-certified, fellowship-trained
13 obstetrician and gynecologist with a comprehensive
14 background in family planning and reproductive
15 health. I'm an abortion provider in the city I
16 call home, the place where I grew up, Washington,
17 DC.

18 As physician providers and experts in family
19 planning, at PRH we believe that the privilege our
20 white coats provide demands that we center those we
21 care for in our work and in our advocacy. It's my
22 honor and my moral duty to provide compassionate

1 care, and in that vein, I'm here to testify in
2 support of my patients, in support of our
3 communities, to ensure equitable access to
4 contraception, including access to birth control
5 pills over the counter.

6 As we reflect on our commitment to care as
7 medical providers, our desire to heal, to treat,
8 and to help, we must also acknowledge that this
9 work, our work, is shaped by the context in which
10 we live and in which our patients live. As
11 healthcare providers and researchers, as public
12 health agents and activists, whose work is focused
13 on addressing health inequities and providing care,
14 when we deeply examine these inequities, it becomes
15 clear that those communities that are impacted
16 greatest by reproductive health inequities and
17 outcomes are also those who have been historically
18 and traditionally marginalized, targeted, and
19 abused by our health care and political systems.

20 This is especially true for those living in
21 my home town of Washington DC, where our political
22 agency and autonomy is routinely usurped and

1 disregarded by ideologically motivated legislators
2 with no ties to or knowledge of our communities.
3 Our communities are made particularly vulnerable to
4 these actions and bear the brunt of restricted
5 access to contraception, as they already face the
6 greatest barriers to accessing care.

7 As a doctor, I know that ensuring equitable
8 access to birth control is essential to the overall
9 health and well-being of people across the country.
10 Reducing barriers to all kinds of care, including
11 contraceptive care, helps address these inequities
12 and reproductive health outcomes, especially in
13 historically oppressed communities. The fact that
14 black indigenous women have the highest rates of
15 maternal morbidity and mortality in this country, a
16 country that spends more per capita on health care
17 than anyone in the world, is not a coincidence. It
18 is the result of centuries of structural and
19 institutional racism.

20 Before I conclude, I would be remiss if I
21 did not stress to you the importance of including
22 young people in this conversation. Research

1 clearly shows that contraindications are rare among
2 adolescents compared to adults, further supporting
3 the safety of OTC access to birth control for young
4 people. The advisory committee has an opportunity
5 to take a critical step to ensuring more equitable
6 access to this essential contraceptive care. I
7 urge you to make Opill available over the counter,
8 free from unnecessary barriers and restrictions.
9 Thank you for having me here today. I look forward
10 to any questions you may have.

11 DR. COYLE: Speaker number 22, please unmute
12 and turn on your webcam. You may begin and
13 introduce yourself by stating your name and any
14 organization you are representing, for the record.

15 MS. EVANS: Greetings. My name is Miyana
16 Evans, and I'm speaking on behalf of Black Women
17 for Wellness to express our support for making
18 birth control accessible to everyone. I have no
19 disclosures to make.

20 As a reproductive, justice-centered, and
21 black women-led organization, Black Women for
22 Wellness is recommending that the FDA vote yes on

1 bringing Opill over the counter. For decades,
2 black women and girls have struggled to control our
3 own reproductive health. We have been silenced,
4 excluded, and misinformed about the uses,
5 effectiveness, and cost of birth control as a means
6 of limiting our agency and controlling the
7 narrative of women's stories.

8 The fundamental tenets of reproductive
9 justice are 1) the right to have children; 2) the
10 right to not have children; and 3) the right to
11 raise those children in a safe and healthy
12 environment. Barriers to accessing birth control
13 are a reproductive injustice, compounded through
14 years of systemic racism. It's hard to say we're
15 at a crisis when it's been bad for so long, but to
16 not call it that is also wrong.

17 In a recent study that Black Women for
18 Wellness conducted, 41 percent of respondents
19 surveyed experienced at least one challenge to
20 accessing contraception in the past year, and
21 59 percent said they will be likely to use an
22 over-the-counter birth control if approved.

1 Instead of having to use and rely on an external
2 entity to decide when, how, and what type of birth
3 control to use, Opill over the counter offers me
4 and my community a safe and highly effective choice
5 of birth control.

6 As a black woman in my early 20s, I
7 unfortunately can say that I have faced barriers in
8 healthcare settings regarding my reproductive
9 health. For too long, I shied away from signing my
10 name on a log to be seen out of fear that I would
11 be judged or seen as irresponsible for seeking
12 control over my reproductive health. I, just like
13 many women, have felt stripped of my power to
14 confidently decide what I felt was best for my
15 body, and ultimately my future.

16 We are taking our power back by breaking
17 through those barriers. Opill, with safe,
18 effective, and actualized support from the FDA, can
19 be accessible and affordable for all women. Making
20 birth control accessible over the counter will
21 eliminate some key barriers such as lack of
22 insurance coverage, transportation restrictions,

1 and racism in the healthcare settings. A yes vote
2 for making birth control pills accessible over the
3 counter is a necessary step in our fight towards
4 full bodily autonomy. We are confident that the
5 FDA can accomplish this by both leveraging the
6 science behind the safety and effectiveness of
7 Opill, and by acknowledging reproductive justice as
8 a basic human right. With gratitude, Black Women
9 for Wellness.

10 DR. COYLE: Speaker number 23, please unmute
11 and turn on your webcam. You may begin and
12 introduce yourself by stating your name and any
13 organizations that you are representing, for the
14 record.

15 MS. MARTIN: Hello. My name is Nicole
16 Martin, and I do not have financial disclosures to
17 make. I speak today on behalf of myself and my
18 organization. I am the co-founder and political
19 education director for Indigenous Woman Rising. My
20 organization is part of the Free the Pill
21 coalition. I also serve as the community co-chair
22 for the New Mexico Department of Health's Maternal

1 Mortality Review Committee.

2 There are barriers to accessing oral
3 contraceptives. For indigenous communities, our
4 healthcare facilities are severely underfunded and
5 not a priority. For many nations, tribes, and
6 pueblos, geography is the biggest barrier to
7 accessing health care. The Navajo Nation, for
8 example, is the size of West Virginia, but only has
9 13 grocery stores and 5 Indian health service care
10 units.

11 AT IWR, we believe in the full spectrum of
12 health care. We believe our relatives and
13 community members deserve safe and equitable
14 access. If there is one thing the federal
15 government can do right, it is to listen to
16 communities that have been oppressed and test
17 subjects for too long. Follow the lead of these
18 communities. These public comments are a
19 reflection of the dire need for us and our
20 community members to maintain control over our
21 bodily autonomy.

22 Opill over the counter is part of the

1 solution because telehealth may not be available in
2 our communities due to the lack of the
3 infrastructure needed to make broadband widely
4 available and affordable; therefore, bringing Opill
5 over the counter is an important step forward. It
6 will eliminate some of the implicit bias we face
7 when we do utilize IHS or other healthcare
8 facilities in border towns.

9 My hope is that if I can go to Walmart and
10 get an eye exam done, I should be able to get my
11 birth control over the counter. I strongly urge
12 the committee to vote yes on bringing Opill over
13 the counter. Thank you.

14 DR. COYLE: Thank you.

15 Speaker number 24, please unmute and turn on
16 your webcam. You may begin and introduce yourself
17 by stating your name and any organizations that you
18 are representing, for the record.

19 MS. BANDELE: My name is Monifa Bandele, and
20 I'm the chief strategy officer at MomsRising. I
21 have no conflicts of interest to disclose. On
22 behalf of over a million MomsRising members, with

1 members in every single state, my testimony today
2 is in support of the switch of Opill from
3 prescription to over-the-counter status. Moms know
4 best about being pregnant and raising children. We
5 know the impact that childbirth has on our bodies,
6 and we know best about whether or not we want to
7 add another child to our family.

8 Birth control pills are popular, safe, and
9 effective methods to prevent unplanned pregnancies.
10 An over-the-counter birth control pill is long
11 overdue. Progestin-only birth control pills have
12 been around for 50 years and are one of the most
13 studied medicines on the market today. They have
14 decades of research and use, showing that they are
15 safe and effective.

16 Opill, like other progestin-only pills, is
17 safe to use for virtually anyone and all women,
18 making them a good candidate for the first
19 over-the-counter birth control pill.

20 Progestin-only pills don't contain estrogen, which
21 means they are safe for women over 35, who smoke,
22 who breastfeed, and who have health conditions such

1 as migraines, blood clots, or heart disease. Women
2 have to see a doctor or pharmacist to get birth
3 control. For parents who don't have much money or
4 people who live in rural areas, visiting the doctor
5 is even harder. There are many extra costs
6 associated with getting a birth control
7 prescription, including paying for a doctor's visit
8 if you don't have insurance, transportation to a
9 doctor's office, missing work, and paying for
10 childcare during a doctor's appointment.

11 Removing the prescription barrier and making
12 birth control pills available over the counter will
13 help make sure that more women have the freedom and
14 access to the contraception they want regardless of
15 who they are, where they live, or how much money
16 they have. It is no wonder that in 2011, a study
17 found that 63 percent of women surveyed were in
18 favor of over-the-counter access, and in 2018, a
19 poll found that 69 percent of parents specifically
20 support making birth control pills available over
21 the counter. MomsRising wants to underscore that
22 progestin-only pills is the only kind of pill that

1 breastfeeding moms can use.

2 The U.S. is in the midst of a maternal
3 health crisis, where black and indigenous women are
4 2 to 3 times more likely to die during childbirth,
5 independent of income and education. More access
6 to birth control will save lives. Bringing Opill
7 over the counter is an important step forward for
8 maternal health and maternal justice. Thank you.

9 DR. COYLE: Thank you.

10 We'll move to speaker number 25. Please
11 unmute and turn on your webcam. Speaker number 25,
12 you may begin and introduce yourself by stating
13 your name and any organization that you are
14 representing, for the record.

15 DR. KAVANAUGH: Good afternoon. My name is
16 Megan Kavanaugh, and I'm a principal research
17 scientist at the Guttmacher Institute, an
18 independent, not-for-profit organization focusing
19 on reproductive health research and policy analysis
20 in the U.S. and globally. I have no financial
21 disclosures to make.

22 I and my colleagues have conducted extensive

1 research examining contraception in the U.S., and
2 evidence generated by us and many other researchers
3 supports the safety of contraception and its
4 centrality in ensuring people of all ages can
5 achieve reproductive health, dignity, and autonomy.
6 Today I want to make five important points about
7 the body of evidence from the behavioral health
8 field that overwhelmingly supports a switch to
9 over-the-counter status for Opill that is inclusive
10 of all ages.

11 1) Young people may have the most to gain
12 from over-the-counter access to contraception.
13 Adolescents experience unique barriers to accessing
14 contraception within the healthcare system,
15 including confidentiality concerns and increased
16 stigma, which would be minimized with broader
17 over-the-counter access to contraception.

18 2) Despite these barriers, most adolescents
19 use contraceptives at both first sex and most
20 recent sex. The most recent available data
21 indicate that three-quarters of females and
22 91 percent of males ages 15 to 19 reported

1 contraceptive use the first time they had sex, and
2 91 percent of females and 94 percent of males
3 reported that they or their partner had used
4 contraception the last time they had sex.

5 3) The science is clear that recent declines
6 in U.S. adolescent pregnancies that occurred too
7 early or were unwanted can be attributed primarily
8 to increases in adolescent contraceptive use.

9 4) Levels of sexual activity among
10 adolescents under age 13 are low and have been
11 declining over time. About 4 percent of
12 adolescents aged 13 and under reported being
13 sexually active in 2015, down from 5.6 percent in
14 2013.

15 5) There is significant evidence from dozens
16 of well conducted studies that increased
17 availability of contraception does not increase
18 sexual activity among young people. Further,
19 between 2008 and 2017, more adolescents were using
20 contraceptives, they were using more effective
21 methods, and they were using them more
22 consistently, all while adolescent sexual activity

1 rates remained unchanged.

2 In short, robust scientific evidence very
3 much supports that over-the-counter access for
4 Opill would have significant benefits for public
5 health and individuals' well-being and should be
6 inclusive of people of all ages. Any age
7 restriction would be counterproductive, as
8 adolescents face both greater chances of unwanted
9 pregnancy, as well as potentially greater
10 ramifications of those pregnancies than adults.

11 I urge the FDA to consider the most current
12 and accurate data available in making an evidence-
13 based decision to make Opill available over the
14 counter without an age restriction. The science
15 overwhelmingly supports a vote of yes. Thank you.

16 DR. COYLE: Speaker number 26, please unmute
17 and turn on your webcam. You may begin and
18 introduce yourself by stating your name and any
19 organization that you are representing, for the
20 record.

21 DR. PARUCHABUTR: Good afternoon. My name
22 is Dr. Komkwuan Paruchabutr, pronouns she/her. I'm

1 speaking on behalf of the National Association of
2 Nurse Practitioners in Women's Health. I have no
3 financial disclosures to make. I'm a
4 board-certified women's health nurse practitioner,
5 family nurse practitioner, and certified nurse
6 midwife and veteran. In short, women's health care
7 is my life's work.

8 I'm here as the president-elect of NPWH, a
9 nonprofit organization that gives voice to over
10 12,000 WHNPs and other advanced practice clinicians
11 that care for women. The clinicians I represent
12 are experts in women's health throughout a
13 patient's entire lifespan. We counsel patients
14 every day on contraception and family planning.
15 The data is clear, and the medical community is in
16 agreement. Contraception is essential health care,
17 and making Opill available over the counter is an
18 important step in promoting health equity improving
19 access to care, and supporting better health
20 outcomes.

21 With my time today, I'd like to emphasize a
22 few important points. As of 2011, 45 percent of

1 pregnancies in the U.S. were unintended. That
2 number is even higher for patients from
3 marginalized communities. Consider the monumental
4 disruption an unintended pregnancy has on a
5 person's life: temporary or permanent delays in
6 education or career; financial instability;
7 long-term lower economic security; and the mental
8 and physical health risks of pregnancy.

9 Hormonal contraception is one of the most
10 widely used and extensively studied medications on
11 the market. Over 60 years of research and data
12 show that it's safe and effective at preventing
13 unintended pregnancies. Over-the-counter access
14 reduces some of the most common barriers to
15 hormonal contraception, such as lack of access,
16 inconveniences of obtaining a prescription, and
17 high costs.

18 We also cannot ignore the current state of
19 sexual and reproductive health care in this
20 conversation. Around 42 percent of unintended
21 pregnancies end in abortion. With the most recent
22 restrictions and bans on abortion and care, an

1 unintended pregnancy carries more risks, harm, and
2 impact than at any other time in the last 50 years.

3 We've been hearing from our members that the
4 rapidly changing policy landscape is interfering
5 with the provision of evidence-based health care
6 and harming patients. With so many aspects of
7 sexual and reproductive health being unnecessarily
8 restricted or eliminated, it's important we remove
9 unnecessary barriers to care.

10 As a clinician, I understand some of the
11 biggest concerns about making hormonal birth
12 control available over the counter are about risk
13 and, yes, there are contraindications, but I'm also
14 confident in the data that shows patients of all
15 ages are capable of self-screening.

16 Research conducted in 2012 and '14 shows us
17 that patients between the ages of 14 and 45 can
18 reliably self-screen and are even overly cautious.
19 In one study, when 6.9 percent of patients reported
20 a potential contraindication to combined hormonal
21 contraception, only 2.4 percent actually had a
22 verified contraindication, and we know from other

1 research that the contraindications are lower, only
2 1.6 percent for progestin-only pills.

3 Self-screening is effective, and we rely on
4 self-screening for so many other medications that
5 have been on the market for decades. As medical
6 professionals who specialize in women's health
7 care, we fully support making Opill available over
8 the counter. Thank you for your time.

9 DR. COYLE: Thank you. We will move on to
10 speaker number 27. Please unmute and turn on your
11 webcam. You may begin and introduce yourself by
12 stating your name and any organization you are
13 representing, for the record.

14 MS. HUITRON: Hello. My name is Dyvia
15 Huitron. I am 19 years old, and I am from McAllen,
16 Texas. When I was 16 years old, I became sexually
17 active. Coming from a very religious community and
18 a household in which sex was discouraged until
19 marriage, I felt as though I was set up for
20 failure. I did not receive the best sex education,
21 but I knew one thing. I could not feel safe and
22 comfortable engaging in this without taking birth

1 control.

2 When I finally mustered the courage to open
3 up to my parents and disclose that I needed a new
4 form of contraception to help me feel safe, I was
5 met with a stern no and a grounding. I was told
6 that if not being given birth control would stop me
7 from being active, then so be it. So I continued
8 having sex without birth control all because I
9 could not access it under the prescription-only
10 system. This was even more likely in my home state
11 of Texas today, as a judge has recently banned
12 young people from getting birth control without
13 parental consent at Title X clinics. Having Opill
14 available over the counter would have solved this
15 problem for me.

16 When I turned 17, I was still sexually
17 active, but my fear of an unintended pregnancy was
18 so much worse, and I revisited the conversation
19 with my parents. This time a new challenge
20 presented itself, the COVID-19 pandemic. For
21 health insurance reasons, I was limited to specific
22 gynecologists that could provide me care, and none

1 of them were taking new patients. For months, I
2 would call the clinics and see if there was any
3 update on the current situation, and I was given
4 the same response each time. "Due to the pandemic,
5 we are currently not taking new patients and only
6 take appointments for emergencies." I felt upset
7 hearing this, and knew that while this particular
8 barrier existed for a viable reason, I was still
9 not able to access the care that I needed.

10 Finally, when I turned 18 and the pandemic
11 slowed down, I was able to set up a visit with my
12 primary care physician to discuss my need for birth
13 control. When revisiting the conversation one last
14 time, I was met with a lot more pushback from my
15 parents, as they simply never felt comfortable with
16 the idea of me taking birth control. They believed
17 it would change my bodily composition, encouraged
18 me to make sexually risky decisions, and other
19 misinformed assumptions.

20 The process that I went through to access
21 birth control does not stop there, as I now live in
22 the state of Alabama, and my university healthcare

1 center reports to my insurance and parents the
2 exams and prescriptions that I'm given. Accessing
3 birth control should not have to be this
4 complicated. At 16, 17, 18, and now 19, my needs
5 have been unmet, yet have remained the same for
6 years. Young people are incredibly intelligent and
7 capable of coming to terms with what their needs
8 are. We should be given the opportunity to make
9 choices for ourselves, regardless of our age,
10 access to care, and background.

11 If birth control was made over the counter
12 in the United States, we would be in a completely
13 different place. I would have felt safer and been
14 able to get what I need on my own terms. My
15 friends who became parents at 18 and 19 could have
16 done so at a time in which they felt more prepared.
17 My peers can make their lives easier and more
18 comfortable on a day-to-day basis, and for this
19 reason, I'm asking you to please consider making
20 birth control over the counter with no age
21 restrictions. It could be life-changing for many
22 of us. Thank you.

1 DR. COYLE: Thank you.

2 We'll move onto speaker number 28. Please
3 unmute and turn on your webcam. Speaker number 28,
4 you may begin and introduce yourself by stating
5 your name and organization you are representing,
6 for the record.

7 MS. BENCOMO: Good afternoon, members of the
8 committee. My name is Charlene Bencomo. I have no
9 financial disclosures to report. I'm the executive
10 director of Bold Features, a state-based
11 reproductive justice organization in New Mexico.
12 We work alongside Latina, black, indigenous, and
13 people of color to ensure that all people have
14 access to the information and resources they need
15 to make informed decisions about their own bodies
16 and lives.

17 For decades, Bold Futures has protected and
18 expanded a full spectrum of reproductive healthcare
19 options with a long history of improving access to
20 contraception in our state. We worked to support
21 the passage of a protocol allowing trained and
22 licensed pharmacists to prescribe contraception at

1 the pharmacy and ushered in the passage of rules
2 related to increased insurance coverage for
3 contraception and pharmaceutical reimbursement
4 parity. While these were all steps towards
5 increased access to contraception for people in New
6 Mexico, evidence still shows that black, indigenous
7 people of color, youth, and LGBTQ people continue
8 to lack access and experience multiple barriers.

9 Bold Futures is a collaborating member of
10 the research team that recently conducted a
11 cross-sectional survey focused on challenges
12 accessing contraceptive care and interest in
13 over-the-counter oral contraceptives among black,
14 indigenous, and people of color. The research
15 tells us what many of us in the large and mostly
16 rural state of New Mexico already know.
17 Contraception is still not accessible to those who
18 need it most, and the effects are disproportionate
19 for people of color.

20 The good news is that 67 percent of
21 respondents stated that they were likely to use an
22 over-the-counter oral contraceptive method if it

1 were available. We know that over-the-counter
2 contraception is both safe and effective. We call
3 on you today to help create additional access and
4 eliminate barriers to contraception by bringing
5 Opill over the counter. Increased access to safe
6 and effective contraception is critical to
7 maintaining bodily autonomy for so many in New
8 Mexico and across the nation, especially as we
9 consider continued attacks on reproductive health
10 care. Thank you.

11 DR. COYLE: Thank you.

12 We'll move on to speaker 29. Speaker
13 number 29, please unmute and turn on your webcam.
14 You may begin and introduce yourself by stating
15 your name and any organization you are
16 representing, for the record.

17 MS. COLEMAN: Clare Coleman, president and
18 CEO of the National Family Planning and
19 Reproductive Health Association. I have no
20 disclosures. I'm speaking today on behalf of
21 NFPRHA, which represents a network of nearly
22 1,000 governmental and nonprofit organizations that

1 provide family planning and sexual health care
2 across the country.

3 Providers in our network rely on Title X and
4 Medicaid funding to subsidize access to
5 contraception for those with low incomes. Federal
6 funding is used to equalize access to birth
7 control, specifically to remove the barrier that
8 cost puts in the way of all people getting the
9 contraceptive of their choice, and more than
10 50 years on, and despite our members' best efforts,
11 millions of people still face significant hurdles
12 to access contraception.

13 I want to speak to the concern about people
14 with low literacy appropriately using an
15 over-the-counter oral contraceptive. People of
16 color and non-native speakers of English have
17 disproportionately lower levels of health literacy.
18 Systemic and structural racism and years of
19 disinvestment, including in safety net healthcare
20 services, lay the groundwork for this and other
21 disparities.

22 Arguments that individuals with low literacy

1 may not be able to read labels and instructions or
2 correctly identify contraindications is a narrative
3 that perpetuates racism and classism. People with
4 low literacy are among those who have the least
5 support and fewest options when it comes to
6 healthcare access. They want and need a
7 nonprescription option. Oral contraceptives are
8 not new products. They do not rely on a new
9 mechanism of action. Over more than 60 years,
10 three generations have shown that people can safely
11 use the pill, accurately understanding the label
12 and eligibility criteria, and taking it once a day
13 for as long as they desire.

14 Opill over the counter would give us one
15 more option for access, and the more options that
16 are available, the better we can make the right
17 choices for ourselves. Those with the power to
18 approve an OTC option must recognize structural
19 barriers are a reality, but not an excuse, to
20 maintain unnecessary restrictions on OTC access.
21 Our health centers will be there for people who
22 need a visit, but for those who know what they

1 want, our providers trust that they can make the
2 right decision for themselves. Our role is to
3 support them in their decision making and get out
4 of their way. I urge the advisory committee to
5 vote yes.

6 DR. COYLE: Thank you.

7 We'll call now on speaker number 30. Please
8 unmute and turn on your webcam. You may begin and
9 introduce yourself by stating your name and any
10 organization you're representing, for the record.

11 MS. CHANCEY: Good afternoon. I'm Leng Leng
12 Chancey, president and CEO of 9 to 5 National
13 Association of Working Women, a nonprofit. I speak
14 on behalf of 9 to 5 and our members, and I have no
15 disclosure to report. I'm speaking today in
16 support of the Opill.

17 9 to 5 is celebrating our 50th anniversary
18 this year. Our work is to end discrimination in
19 the workplace and beyond, and to win paid medical
20 leave, good jobs, higher wages and equal pay,
21 childcare, and more, advancing the growing movement
22 towards a more equitable society. Our members

1 reside in all 50 states. We operate robust
2 statewide chapters in Colorado, Georgia, and
3 Wisconsin.

4 Sixty-three years ago, on this very same
5 day, the FDA approved the first-ever birth control
6 pill. This invention has been hailed as one of the
7 most influential inventions of the 20th century,
8 making it possible for women to leave the kitchen
9 and enter the workplace in great numbers. Thanks
10 in part to the pill, our work force is now over
11 50 percent women, but huge disparities remain due
12 to poverty and structural racism, especially in
13 communities of color. Working women are facing a
14 crisis. The same structural barriers that they
15 face in education, housing, transportation,
16 employment, and childcare are the same barriers
17 they face when trying to access contraception.

18 The public health crisis feeds the economic
19 justice crisis, and vice versa; getting to a
20 doctor, childcare, taking time off, cost,
21 transportation, et cetera. Many of our members are
22 what you might consider low literacy, low-wage

1 working women, but this does not mean they are not
2 savvy about their reproductive health. Working
3 women know the cost of starting and raising family,
4 and it's a really hard cost. They work hard to
5 make ends meet, putting food on the table or paying
6 their light bills. They lean on the community

7 Taking a pill once a day is a culturally
8 well-known fact. Opill is more effective than
9 what's currently available over the counter. Opill
10 is safer economically and physically than being
11 pregnant; and for those living most at the margins,
12 the option of having Opill available over the
13 counter might be the best option they can get.
14 Vote yes to the over-the-counter pill for economic
15 justice and family security. Thank you.

16 DR. COYLE: Speaker number 31, please unmute
17 and turn on your webcam. You may begin and
18 introduce yourself by stating your name and any
19 organization you are representing, for the record.

20 DR. KOYAMA: Good afternoon. My name is
21 Dr. Atsuko Koyama, and I have no financial
22 disclosures. I am triple board-certified in

1 pediatrics, pediatric emergency medicine, and
2 adolescent medicine. I practice in Phoenix,
3 Arizona. I'm a clinician, researcher, and
4 representative of Doctors for America. My research
5 focuses on issues around adolescent reproductive
6 health care in the emergency department or ED. I'm
7 here in support of over-the-counter Opill.

8 I want to start with a patient's story that
9 highlights the importance of adolescent access to
10 Opill. I had a 17 year old come to the ED with
11 concerns around a urinary tract infection, and when
12 I asked her about her sexual and birth control
13 history, she said, "I asked my pediatrician for
14 birth control. He told me I was too young to be
15 having sex, so he wouldn't prescribe it." So
16 despite her being able to access health care and
17 having the courage to even bring it up with her
18 male physician, she was denied birth control
19 because of her doctor's beliefs and biases.

20 I've had way too many conversations with
21 pediatricians and ED docs who don't feel
22 comfortable talking about reproductive health

1 issues with teens, and despite major professional
2 organizations and experts recommending confidential
3 discussions about sex starting at 13 years old,
4 research shows that physicians are failing in this
5 area.

6 Also, the U.S. has the distinction of having
7 one of the highest teen pregnancy rates for a high
8 resource nation. In the past decade, these rates,
9 though still high, have come down due to higher
10 contraceptive use. The average age of sexual
11 initiation is 16 to 17, and an estimated 25 percent
12 of teens have had sex by 18. Of those,
13 approximately 80 percent use some form of
14 contraception, mostly condoms.

15 Of course, hormonal contraception with
16 condom use exponentially improves pregnancy
17 prevention rates, and research also shows that
18 after emergency contraception, or EC, became over
19 the counter, the use of EC among adolescents
20 increased without an increase in rates of
21 adolescent sexual activity. Studies also show that
22 young teens are able to self-screen for potential

1 contraindications to birth control, which are
2 already rare in that age group.

3 I treat plenty of junior high students,
4 13 and 14 year olds who are responsible for their
5 own daily medications, including life-saving meds
6 for conditions like lupus, diabetes, and cancer.
7 For some adolescents, the birth control pill is
8 also life-saving, helping them achieve their
9 educational and life goals.

10 In Arizona, I also see firsthand how
11 restrictions on contraceptive access negatively
12 affect people who are geographically isolated. In
13 fact, more than 19 million women in the U.S. live
14 in contraceptive deserts and don't have regular
15 access to a medical office. Many people who live
16 in rural areas also experience higher rates of
17 poverty and can't afford to travel long distances
18 to obtain a prescription. Over-the-counter birth
19 control access will help these patients.

20 Birth control pills are not the answer for
21 everyone, but having the over-the-counter pill
22 option significantly increases access for patients

1 who already have difficulty finding time, finances,
2 transportation, or a physician willing to speak
3 about and provide contraception; therefore, I urge
4 urge you to make Opill available over the counter
5 free from unnecessary barriers or restrictions.
6 Thank you for having me here today.

7 DR. COYLE: Speaker number 32, please unmute
8 and turn on your webcam. You may begin by stating
9 your name and introducing yourself and any
10 organization that you're representing, for the
11 record.

12 MS. GIBSON: Good afternoon. My name is
13 Candace Gibson, pronouns are she/her, and today I
14 speak on behalf of the National Latina Institute
15 for Reproductive Justice or Latina Institute. I do
16 not have any financial disclosures to make. I am a
17 Latina who has struggled to access contraception, a
18 lawyer, and I have over a decade of experience
19 advocating on behalf of Latinas and Latinxs as they
20 seek sexual reproductive health care.

21 Birth control that's available over the
22 counter can be a powerful tool that will allow

1 Latinas and Latinxs to make meaningful decisions
2 about our lives. In our 2018 poll, 71 percent of
3 Latina and Latina respondents said access to birth
4 control has been important in their own lives,
5 helping them achieve their education and career
6 goals. In the same poll, we found that 78 percent
7 of our community said they would support birth
8 control pills being available over the counter if
9 the FDA found them to be safe and effective.

10 Current barriers prevent Latinas from
11 accessing and affording contraception. Latinas are
12 more likely to work low-wage jobs that do not
13 provide health insurance. Many Latinas who are not
14 citizens of this country cannot obtain public or
15 private coverage due to immigration status. In our
16 2018 poll, we found that nearly 30 percent of
17 Latinas had gone without their preferred method of
18 contraception because of the lack of health
19 insurance. In one study examining the
20 contraceptive method used of Spanish-speaking
21 immigrant Latinas, 82 percent of participants were
22 uninsured.

1 Latinas have reported that providers lack of
2 interpretation and translation services have been
3 the barrier to obtaining contraceptive care, and
4 many in our community cannot even access providers
5 to get a prescription due to lack of
6 transportation, lack of time, and cost. These
7 barriers are especially difficult for rural
8 communities, and these barriers correlate to lower
9 rates of use of contraception for Latinas and
10 adverse reproductive health outcomes.

11 Studies show that Latinas are highly
12 interested in over-the-counter access to oral
13 contraception, noting the cost and convenience as
14 advantages of this option. Decades of research
15 show the efficacy and safety of progestin-only
16 pills. It is critical that over-the-counter
17 contraceptives be covered by insurance, be
18 affordable, and be available without age or
19 documentation requirements.

20 At a time when Latinas are the largest group
21 of women of color to be harmed by state abortion
22 bans, bringing Opill over the counter is an

1 important step forward for Latina and Latinx
2 health, well-being, and self-determination. The
3 Latina Institute urges the advisory committee
4 members to vote yes. Thank you for your time.

5 DR. COYLE: Thank you.

6 We'll move on to speaker 33. Please unmute
7 and turn on your webcam. You may begin and
8 introduce yourself by stating your name and any
9 organization that you're representing, for the
10 record.

11 DR. DHAR: Good afternoon. My name is
12 Dr. Cherie Priya Dhar, and I'm a board-certified
13 adolescent medicine physician, here today
14 representing the Society for Adolescent Health and
15 Medicine or SAHM. SAHM is a nonprofit,
16 multidisciplinary professional society of
17 1200 members committed to the promotion of health,
18 well-being, and equity for all adolescents and
19 young adults, and I have no relevant financial
20 disclosures today.

21 I do want to talk to you about Valerie
22 today, the 16-year-old patient that I never saw.

1 She lived over an hour away, and was told our
2 clinic was the closest that provides birth control
3 to adolescents. Valerie couldn't get to her
4 appointment, as is the case with many teens. SAHM
5 endorses making Opill available over the counter
6 with no age restriction. Let me share with you how
7 this could positively impact our adolescent
8 patients such as Valerie.

9 Oral contraceptive pills, abbreviated as
10 OCPs, are available without prescription in more
11 than 100 countries and have already been used
12 safely by millions of people around the world.
13 OCPs are also the most common contraceptive used by
14 my patients, adolescents. Adolescents have unique
15 barriers to contraceptive access, including those
16 related to transportation, appointment
17 availability, and costs associated with healthcare
18 visits. Like Valerie, in a recent national survey,
19 the overwhelming majority of respondents reported
20 facing at least one barrier to obtaining
21 contraception as a teen or young adult, and because
22 of this, the majority were unable to obtain that

1 prescription.

2 Minoritized adolescents have even more
3 barriers to accessing care. These groups include
4 black, indigenous people of color, recent
5 immigrants, LGBTQ youth, and youth with
6 disabilities, as well as those in more rural
7 neighborhoods. An over-the-counter oral
8 contraceptive would reduce inequities for these
9 young people.

10 This pill is more effective at preventing
11 pregnancy than other over-the-counter
12 contraceptives currently available. Furthermore,
13 per the CDC, for healthy women, no exam or tests
14 are needed before starting progestin-only pills,
15 and mandating such only reduces access to care, as
16 it has for our patient, Valerie. This medication
17 is safe, making over-the-counter status the
18 appropriate way to make it available to the public.
19 In fact, absolute contraindications for
20 progestin-only pills are exceedingly rare in
21 adolescents. Early studies show that many
22 adolescents can understand the Drug Facts Label for

1 this oral contraceptive and that adolescents can
2 self-select for use.

3 Today as members of the FDA advisory
4 committee, you can make a public health impact in
5 increasing access to the state of contraceptives.
6 On behalf of SAHM and Valerie, I urge you to make
7 this available over the counter with no age
8 restriction. Thank you for the opportunity to
9 testify today.

10 DR. COYLE: Thank you, and apologies for any
11 technology issues.

12 I'd like to call on speaker number 34.
13 Please unmute and turn on your webcam. You may
14 begin and introduce yourself by stating your name
15 and any organization you are representing, for the
16 record.

17 MS. NICHOLS: Hello. My name is Victoria
18 Nichols, and I serve as the project director for
19 Free the Pill, a coalition-driven campaign to
20 educate and engage the public in support of
21 over-the-counter birth control pills in the U.S.
22 For nearly two decades, the Free the Pill

1 coalition -- a group of reproductive justice and
2 health advocates, researchers, providers and
3 provider associations, youth activists, and
4 more -- have worked to build the evidence and
5 support for over-the-counter birth control pills.
6 Since the coalition's work started back in 2004, we
7 have been intentional about centering the
8 leadership and perspectives of communities that
9 face the most barriers to accessing contraception
10 due to systemic inequities and those that would
11 likely benefit the most from an OTC birth control
12 pill.

13 Birth control pills are one of the best
14 studied medicines on the market. They have
15 long-standing support from medical and public
16 health experts, and we have decades of data to show
17 that they are safe and effective for people of all
18 ages. Progestin-only pills, the type of birth
19 control pill that the FDA is considering with this
20 application, are safe for nearly all people, making
21 them a good candidate for the first-ever
22 over-the-counter birth control pill.

1 Over 100 countries around the world,
2 including Mexico and the UK, allow people to access
3 birth control pills over the counter without a
4 prescription, and it is time that people in the
5 U.S. have the same level of access. We know that
6 barriers keep birth control pills out of reach for
7 many. Research shows that the current prescription
8 requirement makes it more difficult to obtain and
9 consistently use birth control pills. We also know
10 that barriers to birth control pills fall hardest
11 on black, indigenous, Latinx, Asian American,
12 Native Hawaiian, and Pacific Islander communities,
13 as well as young people, LGBTQ+ folks, people with
14 disabilities, rural communities, and those working
15 to make ends meet.

16 For many, these barriers include finding a
17 healthcare provider; the cost and time associated
18 with a provider visit to get a prescription;
19 transportation; time away from school or work to
20 make the appointment; finding childcare during the
21 appointment if you're a parent; and parental
22 consent for young people. Removing the

1 prescription requirement for birth control pills
2 would expand access to a safe and effective form of
3 birth control for people across the country who
4 want and need it.

5 Today marks Free the Pill Day, a celebratory
6 day in our movement that recognizes the day that
7 FDA approved the first birth control pill in 1960.
8 Now, more than ever, we need equitable access to
9 birth control pills in the U.S. Everyone should
10 have access to the full range of methods so that
11 they can use the one that's best for them.

12 Safe and effective birth control pills
13 available over the counter without a prescription
14 would significantly improve access and help people
15 overcome barriers. I urge the FDA advisory panel
16 to consider the long safety record and broad public
17 health benefits of birth control pills, and vote
18 yes in support of moving them over the counter.
19 This is an opportunity to expand health equity and
20 give people more control over when and whether to
21 start a family and advance reproductive justice.
22 Thank you.

1 DR. COYLE: Thank you.

2 We'll move on to speaker number 35. Please
3 unmute and turn on your webcam. You may begin and
4 introduce yourself by stating your name and any
5 organization that you are representing, for the
6 record.

7 DR. RAFIE: My name is Sally Rafie. I'm a
8 licensed pharmacist and board-certified
9 pharmacotherapy specialist based in San Diego,
10 California. Thank you for the opportunity to
11 address you all and express my support for
12 over-the-counter access to this progestin-only
13 pill. I have seen too many patients attempting to
14 refill their birth control pills at the pharmacy,
15 but having to endure gaps in use while they wait
16 for their healthcare provider to authorize refills
17 or wait for a required office visit. I have no
18 financial interest in the outcome of this meeting.

19 For the last 13 years, I have served as the
20 medication safety specialist for an academic health
21 system. In this role, it is my responsibility to
22 consider the safety of medications and potential

1 for medication errors that may result in patient
2 harm when considering formulary decisions, system
3 design, and staff processes. In addition to this
4 role, I founded Birth Control Pharmacist, a
5 national organization with a mission to expand
6 access to reproductive health services and products
7 and pharmacies. Over the last six years, we have
8 seen more than 1 in 4 states grant pharmacists the
9 authority to prescribe and dispense birth control
10 directly to their patients, and this has been
11 implemented in over 3500 pharmacies.

12 I have personally been providing
13 contraceptive care for over 15 years, and I've
14 trained thousands of health professionals to do the
15 same. While it has been wonderful to see access
16 points to contraception expanding, it's not nearly
17 enough. Even in the states where a pharmacist can
18 prescribe birth control, most do not do so yet.
19 This is a relatively new service that requires
20 pharmacists to undergo additional training and
21 opt-in. In addition to the cost of the birth
22 control itself, patients usually face an

1 out-of-pocket fee for the visit with the
2 pharmacist, as this piece is typically not covered
3 by insurance.

4 During their visit at the pharmacy, the
5 patient completes self-screening that is used by
6 the pharmacist to determine eligibility. In my
7 years of practice, I have yet to see a patient
8 seeking hormonal birth control who has a
9 contraindication to progestin-only pills. I'm
10 confident that people can self-screen to safely use
11 Opill over the counter. We need to be sure that
12 it's available in a variety of ways, including from
13 their healthcare provider, at the pharmacy, and
14 over the counter. With birth control pills, the
15 most common medication error that we see is people
16 taking the pills in the wrong order. Since all the
17 pills in this product are the same, it eliminates
18 any risk of those errors.

19 As a medication safety and reproductive
20 health expert, I am confident that this product is
21 appropriate for nonprescription use and will help
22 improve access to contraception. I urge the

1 advisory committee members to vote yes in support
2 of this application. Thank you again.

3 DR. COYLE: Thank you.

4 We do have a few speakers that are scheduled
5 remaining, so I'll ask our advisory committee
6 members to stick with us here for a few more, and
7 then we'll be wrapping up the agenda for the day
8 shortly.

9 So with that, I'm going to invite speaker 36
10 to unmute and turn on their webcam. You can begin
11 and introduce yourself by stating your name and
12 your organization, if you are representing one, for
13 the record.

14 MS. SCHENK: Good afternoon. My name is
15 Lauren Schenk, and I use she/her and they/them
16 pronouns, and I will be speaking on behalf of
17 myself as a young student with no financial ties.
18 Today, I will be telling you about my first
19 experience with birth control.

20 I went about getting birth control pills for
21 the first time when I was 16. I had to drive over
22 30 minutes to my county's health department two

1 towns over from mine in my home state of Tennessee.
2 I went right after school on the only day that week
3 I was not scheduled to work. This was the only
4 time I could go because the health department is
5 closed on weekends. At the health department, I
6 was very lucky to have been seen by a kind nurse
7 who helped me get the birth control pills, and
8 after we talked, she asked if I had any insurance
9 or a way to pay. I told her that I was
10 uncomfortable with my mom finding out about my sex
11 life, as I came from a very religious household, so
12 she could not know what I was doing. The nurse
13 helped me figure out a way in which I would be able
14 to get birth control pills without having it show
15 up on my insurance or bank statements.

16 Now, I was very lucky that I had a car, had
17 the time, and ability to go to the clinic, and that
18 there was a nurse there who helped me and worked
19 with me to find a way to have birth control, but I
20 am not a common example. Tennessee has one of the
21 highest rates of teen pregnancy in the country
22 because a lot of people I knew did not have even

1 the same limited access to birth control that I
2 did, not to mention the abstinence-only education
3 my school received and the stigma that exists in my
4 community around contraceptives.

5 We should not live in a reality where one of
6 the best case scenarios is a young girl driving out
7 of her way with her limited time to have access to
8 health care. I think we should make birth control
9 over the counter because I think all people deserve
10 access to contraceptives that are safe and
11 effective. Young people in rural areas like me
12 face some of the greatest barriers, so we need
13 access to over-the-counter birth control pills
14 without an age restriction. Thank you.

15 DR. COYLE: Thank you.

16 We will now move to speaker 37. Please
17 unmute and turn on your webcam. You may introduce
18 yourself and begin. Please state your name and any
19 organization that you are representing, for the
20 record.

21 DR. GUPTA: Hello. My name is Dr. Pratima
22 Gupta, and I'm a double board-certified

1 obstetrician/gynecologist based in San Diego,
2 California, and a parent of two young children who
3 had the privilege to plan thanks to access to oral
4 contraceptive pills. I do not have any financial
5 disclosures to make. I'm also a member of the
6 American College of Obstetricians and
7 Gynecologists, but I speak today on behalf of
8 myself.

9 As a doctor, I talk to patients every single
10 day and ensure patient-centered counseling, but
11 personally, even as a doctor, I had trouble
12 accessing oral contraceptive pills when I needed
13 them. Living and working in San Diego, I see many
14 people who are recent immigrants who have
15 self-screened safely and are taking
16 over-the-counter pills obtained, and following the
17 labeling instructions.

18 Let me tell you about a young woman I saw
19 last week. I'll call her Lisa. She had recently
20 immigrated here from Guatemala to San Diego. She
21 needed to get time off of her job as a teacher to
22 come and see me, and she was requesting a refill of

1 a birth control pill that she had obtained over the
2 counter and had been taking without issues. She
3 was confused and, actually, also a bit frustrated
4 that she needed a prescription for a medicine that
5 she'd been taking safely and per the instructions
6 for several years. In fact, she had run out of the
7 pills while she was trying to coordinate the time
8 off to make an appointment. I still remember her
9 sparkly fingernails as she fidgeted due to anxiety
10 of having a delayed prescription.

11 Birth control pills are an important part of
12 the full range of sexual and reproductive health
13 care. This matters to all communities, especially
14 those with language barriers, immigration status,
15 cultural stigma, and low rates of insurance
16 coverage that affect the way they access health
17 care. Over-the-counter access to birth control
18 would alleviate many of these barriers to
19 contraception that our community faces.

20 So how could we have better helped my
21 patient like Lisa and others like her? With
22 over-the-counter access to oral contraceptive pills

1 without barriers, we can be part of the solution.
2 As a doctor who sees patients every week who have
3 been taking over-the-counter oral contraceptive
4 pills without a prescription, I have no doubt that
5 people can take them safely and accurately. Don't
6 leave patients like Lisa worried about a pregnancy
7 when they could be getting progesterone-only pills
8 off the shelf. Bringing Opill over the counter is
9 an important step forward for justice and liberty,
10 upon which this nation was established.

11 I know the last thing that stands between
12 you and a break is me, so I'll wrap it up by urging
13 the advisory committee to be true to the FDA
14 mission and vote yes. Thank you so much.

15 DR. COYLE: Thank you.

16 The open public hearing portion of this
17 meeting has now concluded, and we'll no longer take
18 comments from the audience. I appreciate the
19 committee's time, and we will now turn our
20 attention to address the task at hand, the careful
21 consideration of the data before the committee, as
22 well as the public comments, and this will be the

1 work of our agenda tomorrow.

2 Before we adjourn, are there any last
3 comments from the FDA?

4 (Pause.)

5 DR. HORN: No, we don't have any comment.

6 **Adjournment**

7 DR. COYLE: So hearing none, I will go ahead
8 and just express my appreciation for the work of
9 the committee today in considering and listening to
10 the presentations and the considerable amount of
11 data from both FDA and the sponsor, as well as to
12 the public for contributing their thoughts for our
13 consideration as well. We will now adjourn this
14 meeting. Thank you.

15 (Whereupon, at 5:45 p.m., the meeting was
16 adjourned.)

17

18

19

20

21

22