HBW INSIGHT
CITELINE COMMERCIAL

15 May 2023 | **News**

# Advisory Panel Members On Unanimous Vote Recommending US FDA Approve OTC Birth Control

by Malcolm Spicer

NDAC and ORUDAC members acknowledged the FDA's concerns about some data provided by Opill sponsor HRA Pharma to support its OTC switch application. However, a greater share noted the "historic nature" of the proposal and the broad support expressed in the meeting's public comment portion.

Members of a US Food and Drug Administration advisory panel, to a person, concluded that the potential benefits of OTC sales of a daily oral contraceptive outweigh the risks.

Several agreed with FDA concerns about some data the sponsor of the application for the OTC switch provided, but a larger number noted the historic nature of HRA Pharma's proposal and of their two-day meeting to discussion whether to recommend the agency approve it.

The joint meeting of the Nonprescription Drug and Obstetrics, Reproductive and Urologic Drugs advisory committees conducted online on 9-10 May came 60 years to the month after the first Rx oral contraceptive was approved in the US.

As well, the 0.075-mg norgestrel formulation HRA proposes for OTC sales under the Opill brand was approved for Rx sales in the US in 1973 and remained available through 2005 when the firm discontinued sales as combination

***First OTC Oral Contraceptive Has Advisory Panel's Unanimous Support Despite FDA's Data Concerns***

By Malcolm Spicer

10 May 2023
FDA officials again made clear concerns about "improbable dosing" data in HRA's sNDA for 0.075-mg norgestrel tablet branded Opill

ingredient oral contraceptives claimed dominant market share. The 50-year anniversary of 0.075-mg norgestrel's also wasn't lost on the panel members as they explained their votes on recommending approval.

before advisory panel voted at close of a two-day meeting conducted 60 years after first Rx oral contraceptive approved in US.

*Read the full article here*

Another common statement was appreciation for the consumers and representatives of medical organizations and advocacy groups speaking during the meeting's public comment portion and recommending approval of HRA Pharma's supplemental new drug application. Of the 37 speakers, 35 supported OTC sales of the progestin-only formulation, most imploring the FDA to expand access to birth control for females under 18 years old.

When HRA submitted its switch proposal in July 2022, the deadline under the prescription drug user fee program for the FDA to make a decision on the application was 11 May. Perrigo said the date would be extended 90 days, which will be mid-August, when the FDA in October, after asking HRA to explain the improbable dosing data, postponed the advisory panel meeting originally scheduled for November. (Also see "*US FDA Requests More Information, Needs More Time To Review Birth Control OTC Switch Proposal*" - HBW Insight, 26 Oct, 2022.)

Here, HBW Insight provides, in the order they were asked to vote, excerpts of the statements members made about their reasons for their votes.

**Deborah Armstrong**

"I feel that the risk of unintended pregnancy is lower with this approach than any of the other available contraceptive approaches that our women have access to without seeing a health care provider. I believe that the contraindication to use issues I think will be well understood. And thus, I voted yes.

I would also just like to say that listening to the eloquent and intelligent, informed and passionate individuals, who are mostly young and mostly women who presented at the open public hearing, restores my faith in the future."

JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, DIRECTOR BREAST AND OVARIAN SURVEILLANCE SERVICE, PROFESSOR ONCOLOGY AND OBSTETRICS/GYECOLOGY.
*Source: Source: Johns Hopkins University*

**Kathryn Curtis**

CENTERS FOR DISEASE CONTROL AND

"The evidence demonstrates that the benefits clearly exceed the risks. The benefits of moving a pill over the counter include increased access to contraception, especially those who face multiple barriers that we heard about yesterday, reduction in unintended pregnancy and associated risks and approved reproductive autonomy and improved equitable access to contraception, which we've also heard about so passionately yesterday. So for all of these reasons, I think Opill has the potential there have a huge positive public health impact.

With respect to risks, safety was established 50 years

PREVENTION DIVISION OF REPRODUCTIVE HEALTH WOMEN'S HEALTH AND FERTILITY BRANCH, EPIDEMIOLOGIST *Source: FDA meeting screenshot*

ago when the original approval was made, and the accumulating body of evidence since then, has shown that these pills are safe with very few contraindications and long term safety concerns. With effectiveness also established 50 years ago and while the methods for assessing effectiveness and the population characteristics have changed over the years, all of the estimates that we heard about over the last two days falls somewhere between two and four per 100 which is much lower than any of the other over the counter products and lower than the generally accepted typical use failure rate of seven for oral contraceptives received in the prescription setting. So the large body of evidence on the safety and effectiveness is very reassuring.

The data presented over the last few days from the applicant on comprehension of the label and actual use were also generally reassuring, even with the problems with the data, and even for the subgroups of younger adolescents and those with lower literacy. Those were the two groups that did sometimes have some of the lower scores. Even for these groups, the risk of harm is low and the potential for benefit is high. And that's why I believe that the evidence demonstrates that the benefits exceed the risks."

CASE WESTERN RESERVE UNIVERSITY SCHOOL OF MEDICINE DEPARTMENT OF

**Elma Baron**

"I believe first, when we were asked to serve in this panel, we were asked to scrutinize the evidence, the data that was presented in this study ... and to take into consideration the risks and benefits of having this medication available as an over the counter pill. ... My concerns, number one regarding the breast cancer patient who failed to deselect, was what was most bothersome to me initially. ... I think I have been reassured that this is not normal behavior of the breast cancer population.

Number two concern that I had was the low representation of the low-literacy population and I think the explanation that the [Rapid Estimate of Adult Literacy in Medicine] method or the REALM assessment method could under-detect the low-literacy population and there might actually be more than 14% that's represented in this study. That is

DERMATOLOGY, PROFESSOR; VETERANS AFFAIRS OF NORTHEAST OHIO, CHIEF OF DERMATOLOGY *Case Western Reserve University*

reassuring to me.

I still have questions like most people, about the improbable dosing, but again as a health care provider who lives weighing risks benefit versus benefits on a daily basis, I do think that in this situation, the benefits outweigh the risks."

## Sabrina Everhart

PATIENT REPRESENTATIVE, CHARLESTOWN, IN

*Source: FDA meeting screenshot*

"Thank you to the FDA for the opportunity to be part of this historical review. I did vote yes with adolescent recommendations.

I agree that the adequacy of the safety profile has definitely withstood the test of time and that the [Drug Facts label] is appropriate for over the counter. I understand that for more options and access to reproductive health. I believe the population would benefit from this product over the counter and could safely self-select.

However, I would like to say that I am reserved about the data on adolescent and limited literacy population and their ability to properly make medical choices for this product for themselves without guidance outside of the DFL leaflet. If FDA does not approve this over the counter for these reasons, it could be a reason to consider behind the counter availability. ...

Recommendation could be maybe a public awareness campaign by the sponsor designed specifically for the adolescent population that falls within the over the counter regulations. ...

Finally, I'd like to thank the public for their comments, as it's an important part of my decision process here. As patient representative, I feel like the lack of adolescent and limited literacy studies was my struggle here today. But you also urged us to follow the science that's based on that data presented yesterday and today my recommendation stands of over the counter approval with considerations for young adolescents."

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## Katalin Roth

GEORGE WASHINGTON UNIVERSITY HOSPITAL DIVISION OF GERIATRICS AND PALLIATIVE MEDICINE, PROFESSOR OF MEDICINE; MEMBER GW MEDICAL FACULTY ASSOCIATES *Source: GWU Hospital*

"I agree with almost everything that everyone else has said and so I'll try not to repeat it too much. But I think the safety profile of oral contraceptives since their inception, and of the progesterone-only pills, were very well established. So I think that the public will be well-served from a safety perspective. The risks to women of having an unintended pregnancy are much greater than any of the things we were discussing as risks of putting this pill out over the counter. The history of women's contraception is a struggle for women's control over their reproduction.

I think that the [public comment] speakers yesterday, especially the younger speakers, really brought home to all of us how much more we have to do to repair our broken health system, and how poorly we have made access to health care available for so many young women, adolescents, older women. To the extent that approving this pill to be available over the counter will go towards rectifying that, I think it's a very important move."

## Eve Espey

"I do believe there's adequate information both from the sponsors and from prior evidence that consumers can use a norgestrel safely and effectively. Understanding the methodological concerns, I do believe the sponsors have shown that the single absolute contraindication was well understood and the track record of safety of VIPs for the 30 years that it was on the market is well established.

It would therefore, I think, take a very high bar of concern to justify non-approval of over-the-counter status, given what we know about about this medication.

I also was very moved by the testimony of the public and agree with the strong endorsements of our major professional organizations. My personal experience practicing in a large rural state, New Mexico over the last 30 years. I mean, I see it firsthand, people who face all of these barriers and who also experience the the maternal morbidity and mortality that goes along with unintended pregnancy ... which is highly relevant to this conversation. So from my perspective,

despite the FDA concerns about the study design and different interpretations of the studies, the overall very rare and unlikely harms are outweighed by the tremendous benefits of improved access without any restrictions."

UNIVERSITY OF NEW MEXICO DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, DISTINGUISHED PROFESSOR AND CHAIR

*Source: University of New Mexico*

**Abbey Berenson**

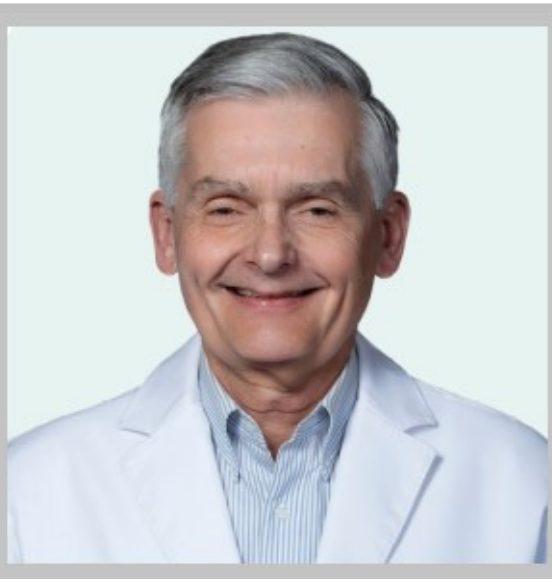
"I felt that both sides did an excellent job of presenting the data and the studies and certainly gave us many issues to think about. Especially with regards to the subpopulations but overall, the data showed that Opill is safe and effective to offer women as an over-the-counter option. And the public comments were very strong in showing the support and the need for this change.

Access is an incredibly important issue to women, especially now, and making this change to over-the-counter hormonal contraception will improve access and allow women to use more effective methods."

DIRECTOR CENTER FOR INTERDISCIPLINARY RESEARCH IN WOMEN'S HEALTH, PROFESSOR DEPARTMENTS OF OBSTETRICS/GYNECOLOGY AND PEDIATRICS, UNIVERSITY OF TEXAS MEDICAL BRANCH GALVESTON *Source: University of Texas Medical Branch Galveston*

**Paul Pisarik**

“I feel the benefits of having a more reliable oral contraceptive upgrade the risks that might be involved in it. I am concerned a little bit about the sub-population sets with limited literacy and adolescents. I'm not quite sure. I'm sure it won't be as effective for them, but it'll still be more effective than what's out there available right now.”



ARCHWELL HEALTH. TULSA, OK, GERIATRIC PHYSICIAN *Source: Archwell Health*

## Maria Coyle

"I also voted yes and support the RX-to-OTC switch for Opill primarily because I think in the balance between benefit and risk, we'd have a hard time justifying not taking this action. The benefits are large, the drug is incredibly effective. I think it will be effective in the over-the-counter realm just as it is in the prescription role particularly given that there may be minimal education occurring currently, even for prescription users of some of this, some of these medications.

Those populations of greatest concern, those with a history of breast cancer or active breast cancer are already highly engaged in the health care system. I think the risk of the medication itself is incredibly low for the vast majority of users, and the risk of unintended pregnancy while real is less than that of existing over-the-counter methods of birth control. Like many of the others panelists here today, I was

(PANEL CHAIR) OHIO STATE UNIVERSITY COLLEGE OF PHARMACY DIVISION OF PHARMACY EDUCATION AND INNOVATION, ASSOCIATE CLINICAL PROFESSOR *Source: FDA meeting screenshot*

incredibly moved by the public hearing comments.

I'm also particularly sensitive to the plight of the FDA having to follow a very stringent process to ensure high quality of our of our medication products, but also in the greater context of where is the best where is the greatest good. On balance, I felt that the OTC switch serves both the public as well as my patients in my own practice settings the best."

## Elise Berlan

"From my perspective as an adolescent medicine pediatrician, I understand that barriers and access to contraceptives are real and very harmful and amplified in adolescents. In these inequities and access perpetuate inequities and communities for neonatal and obstetric morbidity and mortality and also unfairly and unjustly distribute the benefits of contraceptive use. And we should also keep in mind that the health risks of pregnancy, which is the condition that these products into prevent is much greater than the use of any contraceptive product and this is among the safest of the contraceptive products.

Given the evidence presented by the FDA and HRA pharma, the sponsor, I believe that women and pregnancy capable people of all reproductive ages will safely and effectively use the Opill and the potential benefits outweigh the risks of this product.

I also wanted to emphatically state that I do believe that adolescents will make good decisions about the reproductive health and we can trust them to make these decisions. I do recommend that the FDA make a pill available to all women of reproductive age, without delay."

OHIO STATE UNIVERSITY COLLEGE OF MEDICINE DIVISION OF ADOLESCENT MEDICINE, PROFESSOR OF CLINICAL PEDIATRICS; NATIONWIDE CHILDREN'S HOSPITAL, FACULTY PHYSICIAN, COLUMBUS, OH *Source: Nationwide Children's Hospital*

## Marjorie Gass

"I would just like to thank the FDA for considering

NORTH AMERICAN MENOPAUSE SOCIETY EXECUTIVE DIRECTOR EMERITUS; UNIVERSITY OF CINCINNATI COLLEGE OF MEDICINE, CLINICAL PROFESSOR *University of Cincinnati College of Medicine*

this product for over-the-counter use. I think this represents a landmark in our history of women's health. unwanted pregnancies can really derail a woman's life and especially in adolescents' life. I'm very pleased that the FDA is seriously considering this and I look forward to it being on the market."

## Jesse Catlin

CALIFORNIA STATE UNIVERSITY, SACRAMENTO, COLLEGE OF BUSINESS PROFESSOR OF MARKETING

"The comments from the various clinical experts I think clearly indicate that the drug has a favorable safety profile, strong public health benefits. Given my background as a marketing professor, and consumer behavior researcher, I focused a lot of my attention on the consumer studies. Certainly, while there was some very valid concerns, I believe the limitations of the studies were acknowledged and subjected to a very thoughtful analysis by both the sponsor and the FDA. So taken together, the methodological tradeoffs that we know exist in these studies, I think that the results are sufficient to convince me that the benefits of a switch outweigh the risks.

I'd also like to say that I'm hopeful that the FDA approves this, and with the switch that the presence

*California State University, Sacramento*

of an OTC oral contraceptive will lead to improve public knowledge about these products and that they should have a compounding positive impact on consumers ability to use these products safely and effectively. That goes well beyond what we even see here today."

## Susanna Robotti

(CONSUMER REPRESENTATIVE) MEDSHADOW FOUNDATION PRESIDENT, DES ACTION USA EXECUTIVE DIRECTOR, NEW YORK, NY *Source:: FDA meeting screenshot*

"I voted in favor of moving the product from RX to OTC. I support having sponsoring companies meet or exceed or exceed the standards set by the FDA. However, that often doesn't happen in these advisory committees because of mitigating circumstances. With the comprehension for primary selection, deselection and purchase decisions, that research came up pretty well. The areas in which the research seems short have to do with actual use after purchase. I say seems short because we have no research to which we can compare the data we have no proof that women receive complete counseling when prescribed or that they are in a situation where they feel comfortable asking questions. We have no way of knowing that they're better or worse in actual use. ...

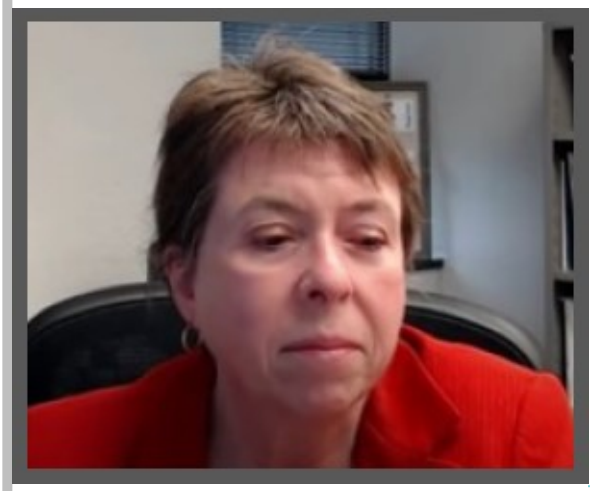
We also know there are a lot more unintended pregnancies than expected if contraceptives were consistently used appropriately, if oral contraceptives were consistently used appropriately. ...

In response to the FDA comment that the sponsor's [actual use study] data was not of a quality that they wanted, even if we had perfect data, without context is it really useful? How to interpret the data with appropriate targets supported by research? was not there. Is anyone here really comfortable with research that has no control group or comparison study? So that was a little bit doomed I feel from the start. I believe those is a mitigating factor and the reason that the uncertain results of the [actual use study] should not impede approval. ...

I found the selecting and deselect results to be acceptable. Access is the most important issue. I was struck by the sponsor's chart on OTC birth control methods versus prescription options. Methods available OTC are less effective. They need participation by both partners and frankly, they also need explanation and even practice to use appropriately. The Opill use instructions are no more difficult to understand and apply than the products available by OTC and the Opill

is much more effective. Pregnancy is a dangerous physical risk in America and should be a choice not a trap. [Progestin-only pills] are more effective than other products offered OTC. More women are likely to be harmed by an unplanned pregnancy and unwanted pregnancy than by the side effects of POP."

## Cynthia Baur



UNIVERSITY OF MARYLAND SCHOOL OF PUBLIC HEALTH HOROWITZ ENDOWED CHAIR IN HEALTH LITERACY, HOROWITZ CENTER FOR HEALTH LITERACY DIRECTOR; PANDEMIC PREPAREDNESS INITIATIVE CO-DIRECTOR; MARYLAND CONSUMER HEALTH INFORMATION HUB DIRECTOR, COLLEGE PARK, MD *Source: FDA meeting screenshot*

"We heard a lot about the drug itself over the last day and a half. The FDA team asked us to think about this really as a risk communication challenge, though, and as a director of a center focused on health literacy, of course I was very interested in the comprehension data and the extent to which comprehension transferred into actions. So do I think that we've got perfect data? No. Do I think it was a perfect study? No. Do I think it was adequate to feel reassured that a large number of people can use this drug as intended? Yes.

I would encourage however, the FDA to continue to raise the bar. They continue to ask sponsors to bring in better data about comprehension. I do want to note that while it is admirable that FDA is focused on limited literacy as one of the special populations, limited literacy and limited health literacy are not the same. It would be really important in future studies to make sure that sponsors are very clear on which populations they're including, which measures they're using and what kind of data they're providing. Overall, I do think as a risk communication situation, the benefits outweigh the risks."

## Pamela Shaw

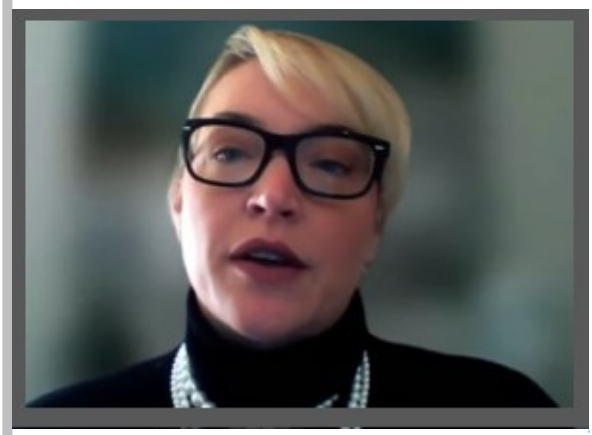
"I think that the benefits outweigh the risks given the overall safety profile of the drug, the good levels of self-selection and the selection particularly for the breast cancer survivors. I acknowledged there were some concerns due to some vulnerable subgroups, the low literacy, the very young adolescents regarding comprehension and whether or not they understood how to use the drug effectively. But I feel

like that the concerns related to lack of access and the consequences there outweighed the concerns pointed out by some of the low literacy challenges on certain questions.

I would like to acknowledge that the difficult position the FDA was put in by the compromised actual use study. But, if the interest of women could be served by getting more data, the FDA feels like they need more data, I hope it can be done in a way that is concurrent with approval and doesn't slow access to this drug. Because I think overall the public statements really helped put this in perspective in terms of the risks were weighing here. I think the benefits do largely outweigh any risks."

KAISER PERMANENTE WASHINGTON HEALTH RESEARCH INSTITUTE ,SEATTLE, BIOSTATISTICS UNIT SENIOR INVESTIGATOR : *Source: Kaiser Permanente Washington Health Research Institute*

## Jolie Haun



JAMES A. HALEY VETERANS' HOSPITAL, TAMPA, RESEARCH SERVICE SUPERVISORY RESEARCH HEALTH SCIENTIST; UNIVERSITY OF UTAH DEPARTMENT OF INTERNAL MEDICINE

"I believe that the efficacy and safety of this birth control form was established over half a century ago and we now have been presented with ample data presenting and demonstrating the effective safe use and benefits of this medication for the people who want to have access to reproductive autonomy.

I do appreciate the scrutiny of the FDA board and I understand that all studies can be improved upon and knowledge base can always be advanced through further investigation.

However, based on what we have available to us at this time, the benefit of Opill being available to diverse populations, including adolescents and those

DIVISION OF EPIDEMIOLOGY ADJUNCT ASSOCIATE PROFESSOR *Source: FDA meeting screenshot*

with limited literacy, is in demand. We do have the data that reflects the ability to make this medication and birth control pill available over the counter. We can take this opportunity to increase access, reduce disparities, and most importantly, increase the reproductive autonomy of the women of our nation."

## Leslie Walker-Harding

UNIVERSITY OF WASHINGTON DEPARTMENT OF PEDIATRICS FORD/MORGAN ENDOWED PROFESSOR AND CHAIR AND ASSOCIATE DEAN; SEATTLE CHILDREN'S HOSPITAL CHIEF ACADEMIC OFFICER AND SENIOR VP *Source: University of Washington*

"I do think even though that this study has limitations, I'd be hard pressed to find a study that won't have limitations considering how it needs to be conducted to get some semblance of resemblance of real world use. I found that what we did find, even with the limitations, was very reassuring that this safe and effective medication can be used by all ages in particular adolescents and those in limited literacy.

With the knowledge that adolescents, even young adolescents make the same decisions that adults make with the medical information given to them, I see no reason to single them out. To not have it available even for the youngest adolescent, especially given adolescents have the lowest risk profile ... given breast cancer is the only contraindication to taking this medication, and that is exceptionally rare in the adolescent age group.

Also, there's no evidence that the risk of using the medication properly is better managed with having a medical professional there. There's no evidence of that and what we do see really affirms that the use is very similar to what we know has happened in the past with prescription medication values with over the counter oral contraceptive prescription use. There I see no reason to withhold this for even the youngest adolescents who can assess when they need that and use it appropriately and if they don't use it appropriately. The safety profile is such that there is very little to no risk with that.

I also think it's very telling that public speaking providers and those here on the voting panel

who care for adolescents and other women who have these need for contraceptives do not want to be a barrier to this do not want to have to be the ones that are withholding a needed medication for women and unable you know there's low access and knowing that you are the barrier to a young person being able to make a decision about their body is very upsetting. I really hope that we can get this approved and over the counter as soon as possible, so that more people aren't harmed by the lack of ability to make a decision on what they want to do with their body."