PUBLIC CITIZEN Health Letter

SIDNEY M. WOLFE, M.D., EDITOR JUNE 2013 – Vol. 29, No. 6

Public Citizen: Oxygen Experiment On Premature Babies Is Highly Unethical

On April 10, 2013, Public Citizen's Health Research Group (HRG) wrote a scathing letter to Secretary of Health and Human Services Kathleen Sebelius condemning a highly unethical government-funded clinical trial involving 1,316 very premature infants. These babies were exposed to an increased risk of blindness, brain damage and death without their parents being informed through the consent forms they signed of these risks or the true purpose and nature of the research. We urged Sebelius to personally apologize to the parents of the critically ill babies enrolled in this high-risk experiment held throughout the U.S. because it was funded by the National Institutes of Health (NIH), the premier research agency within the Department of Health and Human Services (HHS).

The study, known as the Surfactant, Positive Pressure, and Oxygenation Randomized Trial (SUPPORT), was conducted between 2005 and 2009 by approximately two dozen prominent medical research centers throughout the country, including those affiliated with Stanford University; Yale University; Brown University; Duke University; the University of California, San Diego; and the University of Alabama at Birmingham (UAB), which was the lead institution. The participating institutions are part of a multicenter group known as the Neonatal Research Network, which was established in 1986 by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, part of NIH, to conduct research studies on preterm and term newborns.

The failure to disclose critically important information regarding the purpose, nature and risks of the research to parents of the SUPPORT study babies represented an egregious violation of research ethics [that] undoubtedly directly affected parents' decisions to enroll their premature babies in this study.

Overview of oxygen treatment in premature babies

To understand why the conduct of the SUPPORT study was so unethical, one needs to first understand how oxygen therapy is normally administered in premature babies.

Because premature babies have immature lungs, they usually require treatment with supplemental oxygen to survive and to prevent brain damage and other problems caused by oxygen deficiency. In many cases, premature babies also need to undergo intubation (insertion of a breathing tube into the trachea, the main airway leading to the lungs) and treatment with a ventilator (an automated breathing machine). More than 50 years of medical research have demonstrated that for premature babies, treatment with too little oxygen can cause brain injury or death, whereas treatment with too much oxygen can lead to damage to the retina of the eye and blindness.

As part of routine care, the amount of oxygen given to each premature baby is individually adjusted based on a continuous assessment of many clinical factors by the baby's medical team, which includes neonatologists, nurses and a variety of medical specialists. One of the most important factors used to guide oxygen therapy is the oxygen saturation level, a measure of blood oxygen content. Oxygen saturation levels have become so important in the care of critically ill patients that it is sometimes referred to as the "fifth vital sign" (the first four vital signs being pulse, blood pressure, breathing rate and temperature). Since the 1980s, technology has been widely available to monitor oxygen saturation levels continuously using a probe placed

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Terrors of U.S. Drone War Brought to Light

The U.S. use of armed drones against countries around the world is now in its 12th year. President Barack Obama, whose successful 2008 campaign largely relied on discontent with the foreign policy of George W. Bush, has overseen a dramatic expansion of Bush's drone program. While certain commentators rightly railed against Bush for his use of torture and indefinite detention, Obama's similar policies, including his dramatic expansion of the drone killing campaign, have been met with relative silence, or at most exclusive reliance on and deference to administration sources. This indifference has extended to the human impact of the drone wars.

In September 2012, the International Human Rights and Conflict Resolution Clinic of Stanford Law School and the Global Justice Clinic of the New York University (NYU) School of Law released the report "Living Under Drones," which documented the effects of the Bush/Obama policy on the civilian population in Pakistan. The Stanford/NYU report was based on nine months of "… intensive research — including two investigations in Pakistan; more than 130 interviews with victims, witnesses, and experts; and review of thousands of pages of documentation and media reporting... ."

The exhaustive investigation concluded that contrary to official U.S. denials, drones have killed hundreds of civilians in Pakistan alone. Beyond these deaths, however, the report concluded that the drones, which "hover 24 hours a day" over northwest Pakistan, have "terrorize[d] men, women, and children," disrupting whole communities' ways of life and causing widespread psychological trauma.

Escalation of drone war

As the Stanford/NYU report points out, the use of drones in various forms dates back to World War I, but the weapons were used solely for surveillance purposes until 2001. The George W. Bush administration was the first to deploy armed drones on the battlefield in October 2001, during the initial invasion and occupation of Afghanistan, followed by a 2002 strike on six men in Yemen. Strikes on Pakistan began in 2004. (Though the invasion of Afghanistan was illegal under international law, there was at least a formal state of war with that country, unlike with the other countries whose people have been targeted by the weapons.)

Obama's inauguration brought a dramatic escalation in the scale of the attacks. There were 52 drone strikes on Pakistan from 2004 through the end of Bush's term in 2009, but in the subsequent five years, President Obama allegedly launched at least 316 drone strikes on Pakistan, at least 43 on Yemen and three on Somalia. (In the cases of Yemen and Somalia, Obama has not restricted himself to drones. His administration also launched an attack on Yemen in December 2009 that consisted of cruise missiles laden with cluster bombs that killed 41 civilians, including 12 women and 22 children.)

Civilian deaths not aberrations

The Stanford/NYU report notes that the best estimates of the ongoing deaths and injuries caused by U.S. drones come from the Bureau of Investigative Journalism (TBIJ), which has compiled a database of all known drone strikes conducted in Pakistan, Yemen and Somalia since 2004. From the first drone strike in Pakistan in 2004 through May 1, 2013, between 2,541 and 3,533 people were killed by U.S. drones, of which 411 to 884 were civilians, including 168 to 197 children. The Obama administration has been responsible for between 241 and 592 of

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the Pakistani civilian deaths, including 62 to 74 children, through May 1, 2013.

According to a database compiled by *The Guardian*, drone strikes that kill civilians are by no means rare aberrations. Of 337 strikes on Pakistan through August 2, 2012, noted in the database, 79 have resulted in confirmed civilian deaths and 52 others in possible civilian deaths. In another 79 cases, it is unknown whether civilians had been killed. In other words, in only a minority of drone strikes (128, or 38 percent) can it be confirmed that civilians were *not* killed.

Attack details

Though these statistics have been known for some time, the Stanford/NYU report was among the first to give voice to the individuals who have suffered from the attacks. The report described the human aftermath of three such drone strikes at a level of detail rarely reported in the U.S.

The earliest strike described in the report was launched on Jan. 23, 2009, three days after Obama took office. The drone struck an evening gathering of relatives for "tea and conversation" in the home of Mohammad Khalil, a "tribal notable" who may have been targeted because he was reported to be a Taliban sympathizer. According to the report: "At about 5:00 that evening, they heard the hissing sound of a missile and instinctively bent their heads down. The missile slammed into the center of the room, blowing off the ceiling and roof, and shattering all the windows." The strike killed an estimated five to 11 civilians. The only survivor, 14-year old Faheem Quereshi, suffered shrapnel wounds to his abdomen, lost his left eye and hearing in one ear, and suffers from post-traumatic stress disorder (PTSD).

According to the authors, the details of this case raised "… important questions about whether the U.S. complied with basic principles of proportionality and proper precautions in attack." The U.S. had still not formally acknowledged the strike by the time of the report's publication.

The second case focused on a March 2011 strike on a *jirga*, a traditional mechanism for making community decisions or resolving disputes. This *jirga* was convened to resolve a local dispute over a chromite mine, a major source of employment in the region. The apparent impetus for the drone strike was that four of the 40 or so individuals gathered happened to be from a nebulous "local Taliban group" whose presence was deemed necessary to resolve the dispute successfully.

This strike killed an estimated 42 people — mostly civilians — and injured 14 others. As is so often the case, most of those killed were heads of large households, leaving their extended families in the poorest region of Pakistan to fend for themselves. Civilian victims of drone attacks in Pakistan have not been financially compensated by the U.S. government, although federal law authorizes the U.S. to make such payments.

The third strike, launched in June 2011, killed five civilian men in a car: Akram Shah, a father of three; his young student cousin, Sherzada; Atiq-ur-Rehman, a young pharmacist; Irshad Khan, a teenage student working in Rehman's pharmacy; and Umar Khan, the owner of a local auto parts store. More than a year after the strike, the families of the dead men were still suffering in its aftermath.

Indiscriminate strikes

Perhaps the most disturbing part of the Stanford/NYU report describes certain categories of drone strikes that belie the administration's claims that the strikes have been carefully targeted only at individuals known to be actively involved in plotting terrorist attacks against the U.S.

According to the report, the Obama administration conducts two distinct forms of strikes. Personality strikes target specific, named individuals, while signature strikes attack unknown individuals based solely on patterns of behavior that the administration deems suspicious of terrorist activity. Anonymous administration officials cited in a May 2012 *New York Times* article on the drone program complained that the criteria for suspicious activity, which remain a closely guarded secret, are "too lax" (e.g., men loading fertilizer onto a truck could hypothetically be targeted).

Even more disturbing are so-called double-tap attacks. These involve multiple strikes in quick succession on a target, which inevitably includes those who flock to the scene of an initial strike, including rescuers and family members. One eyewitness quoted by the Stanford/NYU investigators described the following strike on the home of his in-laws: "Other people came to check what had happened; they were looking for the children in the beds and then a second drone strike hit those people."

The widespread use of double-tap strikes has led many to avoid rescuing victims of drone strikes for fear of being killed themselves. Even medical first responders in northern Pakistan have instituted policies requiring personnel to wait for up to six hours before attending to victims, resulting in potentially fatal delays in caring for the wounded.

Terrorized civilians

The central aim of the "Living Under Drones" report was to go beyond mere statistics and humanize the public debate, which has previously "focused narrowly on whether strikes are 'doing their job' — i.e., whether the majority of those killed are 'militants'" (a nebulous and all-encompassing term) and to give voice to the "people on the ground who live with the daily presence of lethal drones in their skies and with the constant threat of drone strikes in their communities."

An eyewitness account from former *New York Times* reporter David Rohde, who was kidnapped by the Taliban and held captive in Pakistan for months, described the experience for civilians on the receiving end of the drones:

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on a finger or elsewhere on the skin, which is then connected to a device called a pulse oximeter. All premature babies cared for in neonatal intensive care units (NICUs) in the U.S. have been monitored with these devices for decades.

For the medical centers participating in the SUPPORT study, routine care of premature infants *not in the study* typically involved giving enough oxygen to maintain oxygen saturation levels somewhere within the range of 85 to 95 percent. (Healthy children and adults normally have an oxygen saturation level in the 97 to 99 percent range.) However, within this broad range, the oxygen level target for each premature baby is individually determined at any particular time based on numerous considerations, including:

- diagnostic test results that indicate whether enough oxygen is being delivered to the baby's body (for example, a high blood acid level would indicate insufficient oxygen delivery and the need to increase the oxygen concentration in the air the baby is breathing);
- clinical signs of inadequate oxygen delivery to a particular organ (for example, seizures may suggest that the baby's brain is not receiving enough oxygen); and
- the wishes of the baby's parents regarding the balancing of specific risks (for example, balancing the risk of death with the risk of blindness) and what the parents think would be in the best interests of their baby.

The SUPPORT study oxygenation experiment

The babies in this experiment were extremely premature, having been born at 24 to 28 weeks gestational age and weighing on average less than two pounds. Such babies are critically ill, experience a wide range of complications and have a high mortality rate (although with gradual improvements in neonatology, the survival rate has gradually improved).

The researchers randomly divided these vulnerable subjects into two experimental groups. For one group, the researchers tried to maintain the infants' blood oxygen levels in a low target range (oxygen saturation level of 85 to 89 percent), and for the other group in the more conventional, high target range (oxygen saturation level of 91 to 95 percent), rather than adjust each baby's oxygen levels within the broader range of 85 to 95 percent to meet his or her individual needs as would have been the case had the baby not been in the study. The researchers then measured the impact of the two target ranges of oxygen levels for premature babies — specifically, whether infants in one group were more likely to die, suffer brain damage, or develop eye disease and blindness in comparison to the other group.

It is notable that the SUPPORT study's protocol (a document that includes the rationale for doing the study and a detailed description of the predefined set of procedures for the experiment) stated that the higher oxygen saturation target range was "more conventional" than the lower oxygen saturation target range for the usual standard of care of premature babies. This implicitly means that neonatologists in the U.S. most commonly tried to maintain premature babies in the 91 to 95 percent range at the time the study was conducted.

Another part of the oxygen experiment was the use of specially altered pulse oximeters to monitor the oxygen saturation of the study babies. For babies in the high-oxygen group, the pulse oximeters were intentionally altered to read *inaccurately low*, whereas for babies in the low-oxygen group, they were intentionally altered to read *inaccurately high* whenever their actual oxygen saturation levels were greater than 85 percent or less than 95 percent. For example, when the actual oxygen saturation levels of babies in the low-oxygen group were 85 to 89 percent, the study pulse oximeters indicated the level to be 88 to 92 percent. When the actual oxygen saturation levels of babies in the high-oxygen group were 90 to 95 percent, the study pulse oximeters indicated the level to be 88 to 92 percent. Thus, when the altered pulse oximeters read 90 percent, the actual oxygen saturation level was 87 percent for the low-oxygen group and 93 percent for the high-oxygen group, a clinically significant, 6 percent difference.

The medical teams caring for babies enrolled in the study were only allowed to use these inaccurately reading pulse oximeters when caring for babies in the study. The combined experimental procedure of randomly assigning babies to low or high target oxygen levels without respect to their individual clinical needs, as well as providing intentionally inaccurate information to the entire medical team about blood oxygen levels — a vitally important parameter used to care for babies — represented a considerable deviation from usual standard of care. It is important to know actual oxygen saturation levels because that is a key parameter in deciding when premature babies should be intubated and placed on a ventilator and when they can be safely taken off a ventilator and be allowed to breathe on their own.

Providing the medical team with inaccurate information about oxygen levels could have adversely affected these critical clinical decisions. For example, the inaccurate oxygen level readings could have led the medical team to intubate and artificially ventilate some babies who did not need these medical procedures, thus unnecessarily exposing the babies to the risks of intubation and artificial ventilation. On the other hand, the inaccurate oxygen level readings could have led the medical team to *not* intubate and artificially ventilate other babies who *did* need these medical procedures, thus exposing them to risks of oxygen deficiency.

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For many of the SUPPORT study babies, the overall level of oxygen they received was different from what they would have received had they not participated in the study. Many babies in the low-oxygen group predictably received less oxygen than they would have otherwise received, potentially increasing risk of brain injury and death. On the other hand, many babies in the high-oxygen group predictably received more oxygen than they would have otherwise received, potentially increasing the risk of eye disease and blindness.

Indeed, results of the study published in the *New England Journal of Medicine* revealed that babies in the high-oxygen group were twice as likely to develop the serious eye disease associated with prematurity as those in the low-oxygen group — 18 percent versus 9 percent. Not surprisingly, babies in the low-oxygen group had a higher death rate, with 20 percent of babies in that group dying before discharge compared to 16 percent in the high-oxygen group.

Inadequate consent forms

Given the nature of the experimental interventions in the SUPPORT study and their serious, potentially life-threatening risks, one may wonder how the parents of more than 1,300 premature infants were willing to consent to enrolling their extremely premature infants in this experiment. A review of the final consent forms that were approved by the institutional review board (IRB) — a committee charged with conducting an ethical review of human subjects research — at each study institution reveals that parents were not informed about the true purpose, nature or risks of the study, thereby providing a plausible explanation for why many parents gave their consent.

For example, regarding the purpose of the oxygen experiment, most consent forms simply stated that the study would try to determine whether use of the lower oxygen range would lower the rate of eye disease and blindness. However, all failed to mention that the other primary purpose was to see if babies randomly assigned to the low-oxygen group would have a higher (or lower) death rate in comparison to the high-oxygen group.

The combined experimental procedure of randomly assigning babies to low or high target oxygen levels without respect to their individual clinical needs, as well as providing intentionally inaccurate information to the entire medical team about blood oxygen levels ... represented a considerable deviation from usual standard of care.

When describing the experimental procedures involved in the research, the consent forms in general included language like the following:

> The babies in this study will also be placed randomly (again, like the flip of a coin) into a group monitored with lower oxygen saturation ranges or higher oxygen saturation ranges. Oxygen saturation is measured on a baby with a machine called a pulse oximeter .... The babies in the lower range group will have a target saturation of 85-89%, while the babies in the higher range group will have a target saturation of 91-95%. **All of these saturations are considered normal ranges for premature infants.** If the saturation falls below 85% or goes higher than 95% then the pulse oximeter will alarm so that the doctors and nurses know when to turn your baby's oxygen up or down. [emphasis added]

The short statement that all of these saturations are considered normal ranges for premature infants was very misleading in several regards. First, it failed to communicate to the parents that the higher range was the more conventional range (as was stated in the protocol). Second, it failed to explain the true complexities of oxygen management in premature babies and how oxygen targets are normally individually adjusted based on many clinical factors. Third, and perhaps most important, the consent forms failed to inform parents that the pulse oximeters were altered to intentionally provide inaccurate information across almost all of the 85 to 95 percent range, depriving the entire medical team of accurate information vitally important to the care of premature babies.

Finally, with two exceptions, none of the consent forms disclosed the risks of the experiment comparing high and low oxygen target ranges. Two consent forms noted that babies in the high-oxygen group might have an increased risk of eye damage. Two even went so far as to state, "There is no known risk to your baby from monitoring with the pulse oximeters used for this study." This extremely misleading statement disregarded the risks of brain injury, death and eye disease depending on the randomized group assignment of each baby, instead leading parents to essentially believe there were no risks. It also failed to mention the risks of giving intentionally inaccurate information about the babies' oxygen saturation levels to the medical teams caring for the babies. These included risks associated with either inappropriate delays in intubation or unnecessary intubations. Ironically, the only pulse oximeter risk mentioned — possible skin breakdown — was not even a risk of the research, because these babies needed monitoring with pulse oximeters anyway.

The failure to disclose critically important information regarding the purpose, nature and risks of the research to parents of the SUPPORT study babies represented an egregious violation of research ethics. These

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Sun Protection Is Vital for All

The following article by Dr. Erin Marcus appeared on the website New America Media, www.newamericamedia.org. It is reprinted with permission.

Anyone can get skin cancer, and over the past few decades, the incidence of melanoma, the most aggressive and deadly form of the disease, has increased faster than that of any other form of cancer. Once comparatively rare, melanoma has become the fifth most common type of cancer in men and the seventh most common in women.

The mole on Ivis Febus-Sampayo's face looked odd. But it wasn't until her son needed treatment for acne that she went to a dermatologist. "As mothers, we're working, we're busy," she says. "I forgot about me and called the dermatologist to make sure my son was getting taken care of."

The doctor removed a sliver of Febus-Sampayo's mole and reassured her that it was probably nothing to worry about. Two weeks later, she received a diagnosis she never imagined possible: melanoma.

"I'm of olive complexion, I'm not a sun worshiper, I never baked in the sun, and I don't like the beach," says Febus-Sampayo, a 55-year-old Latina who was born in Spanish Harlem and has spent much of her life in the New York City area. "At no time did I ever think I could have skin cancer."

But anyone can get skin cancer, and over the past few decades, the incidence of melanoma, the most aggressive and deadly form of the disease, has increased faster than that of any other form of cancer. Once comparatively rare, melanoma has become the fifth most common type of cancer in men and the seventh most common in women.

Even though black and Hispanic Americans are less likely to develop melanoma, they are more likely than white non-Hispanics to be diagnosed after the disease has spread and is thus more difficult to treat.

"There's a misconception that if you have darker skin, you will not get melanoma," says Dr. Claudio Dansky Ullmann, a researcher at the National Cancer Institute. "It may be that you are less sensitive or less likely to develop it, but that doesn't mean you aren't going to develop it."

Exposure to ultraviolet radiation from the sun is the biggest risk factor for melanoma and skin cancers generally, and the one that people can do the most to avoid. (Genetics and some skin and immune conditions can increase risk, and some studies suggest that workers exposed to polychlorinated biphenyls (PCBs) may be at increased risk, too.)

Cancer specialists stress that it's important for everyone to protect their skin, regardless of their pigmentation. The American Cancer Society (ACS) promotes a "Slip, Slop, Slap, Wrap" approach — meaning slip on protective clothing (the tighter weave, the better), slop on sunscreen (and re-slather every two hours), slap on a hat (with a two- to three-inch brim all around), and use wrap-around sunglasses that block ultraviolet light (melanoma can start inside the eye, too). The ACS and other groups also recommend minimizing outdoor activities between 10 a.m. and 4 p.m., when the sun's rays are strongest.

There's been some controversy about the safety of sunscreens, and the Food and Drug Administration plans to issue new guidelines on their use later this year. Meanwhile, the Environmental Working Group, a research and advocacy organization that has raised questions about the safety of many sunscreens, has created its own rating system for consumers. For more information, visit www.ewg.org/2012sunscreen/.

Dermatologists have traditionally recommended using sunscreen with an SPF (sun protection factor) of 30 or greater. But Dr. Robert Kirsner, a professor of dermatology at the University of Miami Miller School of Medicine, says that a suncreen's SPF is less important than whether a lotion protects against UVA (ultraviolet A) as well as UVB (ultraviolet B) rays.

Of course, the best protection is to limit time spent in the sun and avoid tanning salons. For people who work outdoors, doctors recommend covering up with a hat, long sleeves and pants and, when possible, staying in the shade.

Another key part of preventing deaths from skin cancer is early detection, since the prognosis is better when the disease is caught early. The American Academy of Dermatology (AAD) urges everyone to get regular skin exams by a medical professional, and the ACS recommends monthly self-exams. For people without health insurance, the AAD organizes free skin screenings, as does the Skin Cancer Foundation.

Many dermatologists recommend using an "ABCDEF" approach to examine skin and urge people to seek medical attention for moles and skin lesions that show one or more of the following characteristics:

- **A**symmetrical shape
- Irregular **b**orders
- More than one **c**olor
- **D**iameter more than 5 millimeters (i.e., about the width of a typical pencil eraser)
- **E**volving, meaning that the suspicious mole or lesion seems to be changing
- **F**unny looking (there is no published research to back up this last point, just common sense)

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Experts also stress the importance of inspecting fingernails and toenails, the soles of the feet, and areas that are normally covered by clothing, such as the groin. Some studies indicate that black people in particular often develop melanomas on the bottom of the feet.

In Febus-Sampayo's case, the melanoma was caught at an early stage. A few days after surgery to remove the growth, she returned to her job as the director of Latina Share, a New York-based support and advocacy group for women with breast and ovarian cancer. She now wears a hat and applies sunscreen every day.

"I think it's really important that people understand you don't have to be fair-skinned, with blue eyes and blonde hair to get skin cancer," she says. "We need to become advocates for our own health, especially in the Latino community, where it's always family first. I always tell women, you need to take care of yourself — if you're not here, you can't take care of them." ✦

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failures undoubtedly directly affected parents' decisions to enroll their premature babies in this study. It is highly likely that had they been appropriately informed, many, if not most, parents would have declined to enroll their babies.

A federal watchdog first identifies consent-form violations

In February and again in March, the Office for Human Research Protections (OHRP), a watchdog division in HHS that oversees human subjects research, sent little-publicized letters to the UAB stating that the study had violated "the regulatory requirements for informed consent, stemming from the failure to describe the reasonably foreseeable risks of blindness, neurological damage and death."

The February OHRP letter to UAB was first brought to Public Citizen's attention when a reporter from a small monthly trade-press publication contacted Dr. Michael Carome, then the deputy director of Public Citizen's Health Research Group (HRG), seeking comment on the letter. (For 10 years prior to joining Public Citizen, Dr. Carome was on the OHRP staff, serving most recently as its associate director for regulatory affairs for eight years).

Actions taken by Public Citizen

After reviewing the OHRP letters and published medical journal articles about the SUPPORT study and related research, it became readily apparent to HRG that not only was OHRP right about the SUPPORT study consent forms failing to disclose serious risks regarding the oxygen experiment, but also that OHRP failed to identify other consent-form deficiencies related to the purpose and nature of the study.

On April 10, after consulting with experts in critical care medicine, pediatrics and ethics, Dr. Carome and Dr. Sidney Wolfe, then the director of HRG, sent a letter urging Sebelius, along with NIH Director Francis Collins, to personally apologize to the parents of the 1,316 babies enrolled in the SUPPORT study because they were never informed — and still may not know — that their babies faced serious danger from the SUPPORT study and that some may have died or suffered from serious eye disease unnecessarily. Public Citizen also called for a broad investigation into the study and other corrective actions and has collected more than 16,000 signatures on a petition with these demands. (The petition can be viewed and supported at http://bit.ly/13MZ06L).

Public Citizen's letter prompted widespread media coverage of the story by outlets ranging from *The New York Times*, *The Washington Post* and the *Wall Street Journal* to National Public Radio, "PBS NewsHour," CNN, "The Diane Rehm Show" and many more.

In a subsequent, April 15 letter to Sebelius, Public Citizen urged HHS to publicly release the protocols and consent forms for seven current and upcoming HHS-funded randomized trials on premature babies being conducted by the Neonatal Research Network — the same group of institutions that conducted the SUPPORT study. Public Citizen also demanded that Sebelius order a suspension of enrollment of infants into these trials until such documents were released and reviewed by independent experts to ensure that the study designs and consent forms were ethical. So far, HHS has not responded to Public Citizen.

In response to the damaging disclosures about the unethical conduct of the SUPPORT study, the investigators and various commenters speaking out in support of the investigators — including the editors of the *New England Journal of Medicine* and some renowned bioethicists — mounted an aggressive campaign to defend the ethics of the study and discredit the findings made by OHRP.

Subsequently in late April, Public Citizen obtained the complete SUPPORT study protocol, followed by the complete IRB-approved consent forms used by at least 22 involved institutions in early May. From these documents, we learned crucial new information about the use of the intentionally inaccurate pulse oximeters and how this unusual experimental procedure posed additional dangers to the babies. In a May 8 letter and report sent to Sebelius, Public Citizen outlined this new information and renewed its request for further action by HHS to address this matter. As this article went to press, a response from the Secretary had not been received. ✦

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"The drones were terrifying. From the ground, it is impossible to determine who or what they are tracking as they circle overhead. The buzz of a distant propeller is a constant reminder of imminent death."

This constant fear has caused widespread psychological trauma. PTSD, with symptoms of anxiety, nightmares and emotional breakdowns, was commonly reported by survivors and witnesses to strikes. Those lucky enough not to have personally experienced a strike experience anticipatory anxiety due to the strikes' unpredictability. With little in the way of mental health treatment available in the area, some have resorted to drastic measures, including tying or locking up those deemed mentally unbalanced. Others reported taking tranquilizers to "save them from the terror of the drones."

The drones have also disrupted normal community life across large swaths of northern Pakistan. Due to the indiscriminate nature of the drone attacks, including "signature" strikes, people have been afraid to gather for weddings, funerals or the all-important *jirgas*, and parents have pulled their children from school for fear of being hit.

These fears are well-founded. Past strikes on schools have killed dozens of children. Obama's first year in office included two strikes on funeral gatherings, one of which occurred eight days after Obama accepted the Nobel Peace Prize. Between 23 and 50 civilians were killed in these two strikes, both of which were deemed "deliberate strikes on funerals and mourners" by TBIJ.

Official denials

President Obama officially denied the drone program's existence for years before finally acknowledging it in an online interview in January 2012. Since then, his administration has attempted at every turn to downplay civilian casualties, with a senior administration official putting the total number of Pakistani civilians killed by drones in the "single digits." Obama has claimed that while civilians had indeed been killed by drone strikes, it was not "a huge number," maintaining that his drone policy was a "targeted, focused effort."

Obama's claims of a low number of civilian casualties are in part due to his administration's shrewd bookkeeping minimizing the appearance of civilian harm. According to *The New York Times*, Obama considers "all military age males in a strike zone as combatants … unless there is explicit intelligence posthumously proving them innocent." Other victims, including women and children, are — like the program itself for years — simply unacknowledged.

International law ignored

Obama's quiet but dramatic escalation of drone attacks on Pakistan, Yemen and Somalia has merited scant or subdued criticism from the mainstream media, contributing to a perception that the weapons constitute a low-risk, precise, necessary evil to combat terrorism. Perhaps as a result, the program has consistently enjoyed majority support among the American public, including Democrats.

Some criticize the drone policy on procedural rather than substantive grounds, decrying the lack of transparency surrounding the strikes or advocating that all strikes be conducted by the U.S. military rather than the CIA, but accept that civilian casualties, while tragic, are an unintended consequence of an otherwise necessary policy.

Ignored in such debates is that international law only allows an attack on another country's territory if United Nations authorization is granted or if conducted in self-defense, traditionally defined as an armed attack that is "instant, overwhelming, and leaving no choice of means, and no moment of deliberation." The drone policy does not meet these conditions because the U.S. has never pursued international authorization of the program, and the Obama administration revealed in a recently released white paper that it does not restrict its strikes only to situations involving immediate threats of armed attack.

Even if international law permitted such attacks, however, what is legal for one country would be legal for all. Logically speaking, supporters of the right of the U.S. to carry out its drone program are essentially advocating for the right of other countries to wield drones of their own against self-described "threats" around the world, including some in the U.S. This is clearly not the intention of supporters of U.S. drone strikes, yet this obvious implication is rarely discussed.

Equally ominous implications are found in Pakistani views on the strikes. Although rarely reported here, a 2010 Pew poll found that only 23 percent of Pakistanis approved of the drone strikes at that time. Predictably, the number of Pakistanis who view the U.S. as an enemy steadily rose from 64 percent in 2009 to 74 percent by 2012. Approval of the strikes also slid further, to 17 percent, by 2012.

Attacks continue unabated

The recent confirmation of John Brennan, one of the architects of the drone program under President George W. Bush, as head of the Central Intelligence Agency met with bipartisan support (notwithstanding Senator Rand Paul's historic filibuster) and enjoyed little attention from the media beyond the initial Senate confirmation hearings. Despite public gestures from the administration to increase the transparency of the program, drone strikes continue unabated under a shroud of secrecy, with 12 strikes already launched on Pakistan in the first four months of 2013. It remains to be seen how many more thousands will die or continue to live in a state of perpetual dread before Obama hands the trigger to his successor. ✦

HRG Works for You!

Our latest work involves dangerous and inadequate oversight of compounding pharmacies and unethical testing on premature babies

The work of Public Citizen's Health Research Group (HRG) doesn't end with its *Health Letter* and *Worst Pills, Best Pills News* publications. HRG uses our own research, current academic research, government data and information from whistle-blowers to advocate for consumers by:

- petitioning the government to remove unsafe drugs or medical devices from the market, and to require warnings of dangerous side effects on other drugs;
- testifying before government committees and arguing against approval of unsafe or ineffective drugs and medical devices;
- writing letters to government agencies about the adverse effects of drugs and medical devices; and
- urging Congress to strengthen the regulatory oversight of drugs and medical devices.

Our latest research-based consumer advocacy includes:

- **Public Citizen Report Documents Lack of Informed Consent for Risky Study on Premature Babies — 5/8/2013** — In a report submitted to Secretary of Health and Human Services Kathleen Sebelius, Public Citizen presents an independent analysis of the complete protocol and informed consent documents for the SUPPORT study involving extremely premature babies. The key finding in the report is that parents of babies enrolled in the study were not told the dangers of the study's experimental procedures.
- **Public Citizen's Comments on Senate HELP Committee Draft Proposal for Regulatory Oversight of Compounding Pharmacies — 5/3/2013 —** Public Citizen expresses grave concerns with the Senate HELP Committee's draft legislative proposal that would weaken the existing laws governing drug manufacturing. The legislation would create an entirely new regulatory class of drug manufacturers that would be subject to substandard requirements for ensuring the efficacy, safety, quality and labeling of drugs.
- **Letter to Food and Drug Administration Demanding Explanation for Dangerous Delay Between Identifying Problems and Publicly Recalling Potentially Contaminated Products Distributed by Balanced Solutions Compounding Pharmacy — 4/22/2013 —** Public Citizen requests an explanation for the unacceptable one-month delay between the Food and Drug Administration's (FDA's) inspection of Axium Healthcare Pharmacy (doing business as Balanced Solutions Compounding Pharmacy), which was finished on March 15, 2013, and identified serious quality control problems related to the production of sterile drugs, and the subsequent nationwide voluntary recall of all lots of sterile products compounded by this pharmacy on April 17, 2013.
- **Letter to the Assistant Secretary for Health and the Office for Human Research Protections Director Regarding Neonatal Research Network Trials — 4/18/2013 —** Public Citizen requests emergency action by the Office for Human Research Protections (OHRP) to ensure that newborn premature and term infants are being adequately protected in seven current randomized trials being conducted by the Neonatal Research Network (NRN).

Visit www.citizen.org/hrgpublications to read full reports and testimonies as HRG fights for government and industry accountability in the interest of the public's health.

Product Recalls

April 3, 2013 – April 30, 2013

This section includes recalls from the Food and Drug Administration (FDA) Enforcement Report for drugs and dietary supplements (www.fda.gov/Safety/Recalls/EnforcementReports/default.htm), and Consumer Product Safety Commission (CPSC) recalls of consumer products.

DRUGS AND DIETARY SUPPLEMENTS

Recalls and Field Corrections: Drugs – Class I

Indicates a problem that may cause serious injury or death

Actra-SX, 500 Capsules, Maximum Strength Energizer, 500 mg, 5 count package. Volume of product in commerce: 30,000 capsules. Marketed without an approved NDA/ANDA: Product contains sildenafil, an active ingredient in a FDA-approved product for the treatment of erectile dysfunction. Lot #: 008A, expiration date 12/14. Body Basics Inc.

Blue Male Enhancement Pill, bulk product. Volume of product in commerce: 50,000 capsules. Marketed without an approved NDA/ANDA: Product found to contain sulfoaildenafil, an analogue of sildenafil, the active ingredient in an FDA-approved product used for erectile dysfunction, making it an unapproved new drug. Lot #s not specified. The Menz Club, LLC.

Recalls and Field Corrections: Drugs – Class II

Indicates a problem that may cause temporary or reversible health effects; unlikely to cause serious injury or death

Ciprofloxacin Tablets USP, 500 mg, 100-count bottle. Volume of product in commerce: 7,136 units. Presence of foreign substance(s): A complaint was received for a rubber-like material in a 500-mg ciprofloxacin tablet. Lot #: CB222A, expiration date 06/16. West-ward Pharmaceutical Corp.

Clonazepam Orally Disintegrating Tablets, USP, 0.5 mg, 60 tablets (10 blister cards of 6 tablets each). Volume of product in commerce: 3 boxes. Failed content uniformity specifications: Recall is being carried out due to an out-of-specification result for content uniformity. Lot #: 32900136A, expiration date 05/14. Teva Pharmaceuticals USA, Inc.

Ethambutol Hydrochloride Tablets, USP, 100 mg, 100-count tablets per bottle. Volume of product in commerce: 3,061 bottles. Out-of-specification results for assay at the stability time-point of 24 months. Lot #: 68028A, expiration date 07/14. West-ward Pharmaceutical Corp.

Levoxyl (levothyroxine sodium) Tablets. Multiple dosages, quantities and lots affected. Contact your pharmacist. Chemical contamination: emission of strong odor after package was opened. Pfizer Inc.

Lisinopril and Hydrochlorothiazide Tablets, USP, 20 mg/25 mg, 100- (NDC 60429-046-01) and 1,000- (NDC 60429-046-10) count bottles. Volume of product in commerce: 6,158 bottles. Presence of foreign substance: Reports of gray smudges identified as minute stainless steel particulates were found in the recalled tablets by the manufacturer. Multiple lots affected. GSMS Inc.

Physicians Total Care Tetracycline, 250 mg, 30-capsule bottle. Volume of product in commerce: 1,200 capsules. Presence of foreign substance(s): There is a potential for foreign particulate matter in the API. Lot #s: 69MO, expiration date 05/13; 69SH, expiration date 05/13; 5KXZ, expiration date 05/12; 5RE1, expiration date 05/12. Physicians Total Care, Inc.

Physicians Total Care Tetracycline, 500 mg, 30-capsule bottle. Volume of product in commerce: 3,660 capsules. Presence of foreign substance(s): There is a potential for foreign particulate matter in the API. Multiple lots affected. Physicians Total Care, Inc.

Venlafaxine Hydrochloride Tablets, 75 mg, 100-count tablets per bottle. Volume of product in commerce: 13,320 bottles. Failed tablet/capsule specifications: Pharmacist complaint of an excessive amount of broken and/or chipped tablets in the bottle. Lot #: MM8490, expiration date 09/14. Zydus Pharmaceuticals USA Inc.

CONSUMER PRODUCTS

Contact the Consumer Product Safety Commission (CPSC) for specific instructions or return the item to the place of purchase for a refund. For additional information from the CPSC, call its hotline at (800) 638-2772. The CPSC website is www.cpsc.gov. Visit www.recalls.gov for information about FDA recalls and recalls issued by other government agencies.

Name of Product; Problem; Recall Information

12-Volt Heated Jacket Liners. A defective wire connector can cause the jacket liner to overheat, posing a burn hazard to consumers. Gerbings LLC at (877) 242-5595 or www.gerbing.com.

100-Pound Propane Cylinders. Fuel can leak from the thread connection between the cylinder and valve, posing a fire hazard if exposed to an ignition source. Manchester Tank & Equipment Co. at (800) 640-6327 or www.mantank.com.

2012 Huffy® 20-Inch Slider Tricycle. The handlebar can unexpectedly loosen while in use, causing the rider to lose control. This poses crash and fall hazards for the rider. Huffy at (888) 366-3828
or www.huffybikes.com.

"Aubree's" and "Hearts" Baby Socks. The flowers and the bows on the baby socks can detach, posing a choking hazard to young children. Trumpette, Inc. at (877) 938-7265 or www.trumpette.com.

Buckyballs and Buckycubes High-Powered Magnet Sets. These products contain defects in the design, warnings and instructions, which pose a substantial risk of injury and death to children and teenagers. Multiple retailers.

CE Tech 1,000 ft. Riser Cable. The riser cable does not meet fire resistance standards for riser cable, posing a fire hazard. Home Depot at (800) 394-7519 or www.homedepot.com.

Chandeliers. Defective wiring can conduct electricity to the chandeliers' metal parts, posing an electric shock hazard to consumers. Currey & Company at (866) 577-6430 or www.curreyco.com.

Children's Wooden Puzzles. Small pegs on the puzzle boards can loosen and separate from the boards, posing a choking hazard to children. Small World Toys at (800) 421-4153 or www.smallworldtoys.com.

Compact and Large Handgun Security Vaults. The lock can fail and allow unintended access to the contents of the vault. Battenfeld Technologies Inc. at (877) 509-9160 or www.lockdownvaults.com.

Dollies. The hands on the plush dolls can detach, posing a choking hazard to young children. The Land of Nod at (800) 933-9904
or www.landofnod.com.

Floor Lamps. A failure of the lamp's joint locking mechanisms can cause the lamp to collapse and the electrical cord to spark, posing injury and shock hazards to consumers. West Elm at (855) 776-6953 or www.westelm.com.

Giada De Laurentiis Ceramic 9x13 Inch Lasagna Pan. The pan can break causing sharp edges and posing a laceration hazard. Target at (800) 440-0680 or www.target.com.

Gingham Bunny Forks and Spoons for Babies. The pink coloring on the bunny's ears can come off, posing choking and ingestion hazards to babies. Reed and Barton Corp. at (800) 343-1383 or www.reedandbarton.com.

Girl's Three-Piece Clothing Sets. The vest sold with these sets has a belt at the waist that could become snagged or caught in small spaces or vehicle doors and it poses an entanglement hazard. Children's Apparel Network at (800) 919-1917 or www.childrensapparelnetwork.com.

High-Pressure Scuba Diving Air Hoses. The diving hose that connects the regulator to the tank's pressure gauge can leak, posing a drowning hazard to the user. Trident Diving Equipment at (800) 234-348 or www.TridentDive.com.

Infant Froggy Socks. The stitched knit frog face and feet on the socks can detach, posing a choking hazard to infants and young children. Classic Characters at (877) 298-9620 or www.classiccharacters.com.

Mini Boden Chunky Cord Dungarees. The studs and clasps on the pants can detach, posing a choking hazard to infants and small children. J.P. Boden Services Inc. at (866) 206-9508
or www.bodenusa.com.

One-Piece Footed Infant Clothing with a Zipper. The zipper pull can detach, posing a choking hazard to young children. Carter's, Inc. at (888) 282-4674 or www.Carters.com.

Urban Shredder Ride-On Toys. Toys can unexpectedly accelerate and cause the rider to lose control, posing a fall hazard. Dynacraft at (800) 551-0032 or www.dynacraftbike.com.

PUBLICCITIZEN Health Letter

Outrage of the Month: Medicare Advantage — Whose Advantage?

Is one purpose of increasing government funding of Medicare Advantage (MA) to enhance stock value — to the benefit of stockholders — of large, for-profit MA companies such as United Health and Humana?

In April 2013, the Centers for Medicare & Medicaid Services (CMS, part of the Department of Health and Human Services [HHS]), announced that it would pay even more to already overpaid MA companies. As our colleagues at Physicians for a National Health Program (PNHP) revealed, the announcement of the $71.5 billion [over the next 10 years] gift to MA companies resulted in top insurers' shares gaining $13.2 billion in one week.

As you may know, MA (also known as Medicare HMOs) is a for-profit alternative to traditional Medicare in which the government pays private insurers on an annual, per capita basis for the care they deliver to the Medicare recipients choosing these plans. The insurers have essentially gamed the system by making it appear that the patients for whom they get reimbursed are sicker and at higher risk, and therefore merit larger government payouts, than is often the case. A January 2013 study by the Government Accountability Office titled "Substantial Excess Payments Underscore Need for CMS to Improve Accuracy of Risk Score Adjustments" documents the waste of government dollars to the benefit of private MA insurers.

President Obama had called for cuts in overpayment under the Affordable Care Act. But as PNHP cofounder Dr. David Himmelstein states, "April's extraordinary rate-setting directive from [HHS] Secretary Kathleen Sebelius to [CMS], in which she spurned historical practice and the advice of the CMS Office of the Actuary, will result in an obscene windfall to the private, for-profit insurers.... This backroom Medicare giveaway is a heavy blow to taxpayers and the traditional, public Medicare program."

According to PNHP research, selective enrollment of healthier seniors was the major source of excess payments to these plans before 2004. That year, Medicare adopted a risk-adjustment scheme, but ineffectively: $122.5 billion have been added to Medicare's costs since 2004. The PNHP researchers conclude, "It is time to end Medicare's costly experiment with privatization. The U.S. needs to adopt a single-payer national health insurance program with effective methods for controlling costs." We strongly agree.

PUBLICCITIZEN
Health Letter, Public Citizen Health Research Group
1600 20th Street NW, Washington, DC 20009

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