Biotechnology has played a key role in the development of vaccines and continues to help develop different vaccines everyday. Vaccines are used today not only to prevent multiple epidemics, which once were a major worldwide concern, but also to prevent childhood diseases, sexually transmitted diseases, and the flu. One recently approved vaccine stirring up a lot of controversy is Gardasil®. Multiple disciplines of public officials have been arguing about whether Gardasil should be mandated in a specific population of females in order to end school. This paper will address what Gardasil is and the role it has, the pros and cons of mandating the vaccine, the views of parents, health care professionals and religious groups regarding the mandation of the vaccine, and the ethical issues involved in this decision.

Gardasil is a vaccine that was approved in June 2006 to help prevent diseases caused by the human papilloma virus (HPV) Types 6, 11, 16, and 18. There are over 100 strands of the HPV, of which 30 have been found to be involved in sexually transmitted infections. This vaccine helps form antibodies against the most commonly transmitted virus strands. This is an important fact to keep in mind when discussing whether the vaccine should be mandated. It does not protect individuals against all strands of HPV, only the four most common. This has been an issue to some parenting groups that have expressed concern that teenagers might think they are one hundred percent covered against HPV when in fact they are not. The two diseases the vaccine helps reduce are cervical cancer and genital warts. HPV Types 16 and 18 cause approximately 70% of cervical cancer cases while HPV Types 6 and 11 cause 90% of genital warts. Cervical cancer occurs when a female contracts certain types of the virus and it does not go away on its own. This occurs in approximately 10% of females infected. Abnormal cells then develop in the lining of the cervix and if not discovered and treated early into the disease state the abnormal cells can lead to precancerous cell lines and eventually cervical cancer. It is estimated that there are 10,000 new cases of cervical cancer each year in the United States and 3,700 deaths from cervical cancer. This makes cervical cancer the second leading cause of cancer deaths in women worldwide. Genital warts are caused by a similar mechanism to cervical cancer; a female will receive the virus from a sexual partner either through skin to skin contact of the genital area, oral sex, or intercourse. Two thirds of individuals who contact the specific type of HPV that causes genital warts will get them and if treated, 25% of individuals have a re-infection within three months indicating the virus is still present. This is the main reason of high transmission rates, the virus can be transferred unknowingly through asymptomatic individuals. The Center of Disease Control (CDC) has estimated that 20 million people in the United States had HPV in 2005 with approximately 6 million new cases of genital HPV occurring every year. The CDC has also estimated that 74% of new cases occur in individuals 15 to 24 years of age, approximately 9.2 million individuals, which means the vaccine should be targeted at individuals younger than 15 years old.

After review by the Food and Drug Administration (FDA) the vaccine has been recommended in girls and women aged nine to twenty-six years of age. The vaccine is most efficacious when given before an individual has contact with HPV Types 6, 11, 16, and 18 meaning that the younger vaccinated the more protection the vaccine will give. The vaccine has a complex administration schedule, 3 injections over six months, which has caused difficulty for physicians in trying to get the patients to come back for the second and third shot. Studies have now found that patients may benefit from Gardasil if they already have HPV. This is due to the fact that most people are not infected with all four types of HPV that the virus contains. In clinical trials, individuals with current or past infection with one or more vaccine-related HPV types prior to vaccination were protected from disease caused by
the remaining vaccine HPV types. For example, if an individual is found to have contracted HPV Type 6 and then they receive the vaccine, they will acquire protection for Types 11, 16, and 18. This study helped the Advisory Committee on Immunization Practices (ACIP) vote unanimously to recommend that girls and women 9 to 26 years of age be vaccinated with Gardasil. This decision carries a huge impact not only financially for Merck but also on the United States female population. This will be the first vaccine ever to help prevent sexually transmitted diseases and cancer. The goal of the ACIP is to decrease the number of females who contract these HPV strands thereby decreasing the spread to males who may have eventually infected more females. The decision made by the ACIP prompted the CDC to add Gardasil to the Vaccines for Children (VFC) program, which pays the cost for vaccination in children who are Medicaid eligible, uninsured, underinsured or Native American. This decision is predicated to cost the federal government two billion dollars due to the vaccine being the most expensive of the 16 vaccines on the immunization schedule and the three shots combined cost approximately three hundred and sixty dollars. Overall, this cost is predicated to be less than the health expenses related to carrying for individuals with cervical cancer and genital warts. Individuals older than 19, and not covered under the VFC program, can obtain financial assistance for the vaccination from Merck & Co., the manufacturers of Gardasil. Older women are still encouraged to get vaccinated since at least 80% of sexually active women in the United States will have acquired a genital HPV infection by fifty years of age.

Soon after Gardasil was approved by the FDA, there was a lot of debate among parents, health care professionals and religious groups regarding whether the vaccine should be mandated in school aged children in order to continue to attend school. When a poll was taken of parents, 80% said they would vaccinate their daughter under 15 years of age. The main concern parents have is the idea that their children will not understand at such a young age, between eleven and twelve years old, the vaccine does not prevent all sexually transmitted infections (STIs) or even all types of genital warts. Parents have a fear that their children will assume that, since they have been vaccinated, they can engage in more sexual activity without worrying about contracting an STI. The CDC has referred to this type of behavior as “disinhibition,” meaning, “an increase in unsafe behavior in response to perceptions of safety caused by introduction of a preventive or therapeutic intervention.” It is understood by most parents that the vaccine is extremely beneficial in regards to decreasing deaths from cervical cancer and cases of genital warts from asymptomatic sexual partners but parents question as to why it has to be administered at such a young age. With further education of parents and children the vaccine can have a positive role. Parents and health care professionals can educate their children once they reach an older age that they were vaccinated for a virus that causes some, not all, types of cervical cancer and genital warts but there are still multiple other viruses and diseases that can be transmitted sexually that the virus does not protect for. Parents can also be educated in regards to why the vaccine has to be administered at such an early age. Health care professionals such as physicians and pharmacists can explain to parents that the vaccine is only 100% effective if administered before any contact of the four HPV viruses in the vaccine. The decrease in efficacy of the vaccine after sexual activity should be enforced to parents to help them make an educated decision when deciding whether or not to vaccinate their daughter. Studies have also determined that the sexual activity of participants in the study did not increase after vaccination indicating that teenagers may not feel they can be more promiscuous. Most teenagers with proper education will realize there are multiple, deadly diseases such as HIV and hepatitis that can be transmitted sexually which they are not protected against. Teenagers can be taught to remain abstinent until marriage, get to know their sexual partners, be tested, and practice safe sex methods such as condoms. With media advertising by the drug company, and in depth conversations with
health care professionals I think parents will express less fear of having their daughter vaccinated.

The decision to vaccinate ultimately is up to parents and guardians who have the power to determine the effectiveness of a vaccine based on the amount of individuals vaccinated. "Immunization can only be effective if eligible individuals or their legal representatives (e.g., parents or guardians) agree to its use" (Parental Beliefs). Studies have shown that multiple factors influence a parents decision to vaccinate their child for a specific disease state such as, "social-environmental factors, parent-specific or personal factors, the family's interface with the health care system, institutional policies and interventions related to vaccines, and the physical environment of health." Social-environmental factors include individual's personal and cultural beliefs regarding vaccination itself and the disease the vaccine is used for, as well as involvement in certain groups such as antivaccination or religious affiliations. Parent specific or personal factors are basically the perceptions the parent holds on the disease state, and the efficacy and safety of the vaccine. There are two major factors that are related to the family’s interface with the health care system; the first being the health care provider’s attitude and beliefs. Parents rely a lot on the opinion of their health care provider in order to make health care decisions for their children. If a health care provider presents a negative attitude regarding a vaccine either due to personal beliefs or past experience with a particular vaccine that negative energy will come across to the parent and influence his or her decision. The second factor involved in the family’s interface with the health care system is the access to health care and the vaccine in particular. Vaccine cost and availability often influence a parent’s decision regarding whether to vaccinate their child. This is a sad situation because no child should go unvaccinated due to the cost associated with the vaccine. This problem thankfully is solved in the United States with the Vaccination for Children program described above. Even with this program offered in the United States, "between 1995 and 2000, the estimated numbers of unvaccinated children between the ages of 19 and 35 months significantly increased in the United States. In this age group, 36.9% were undervaccinated and 0.3% had not received any vaccines." Hopefully, in the future, with more positive media advertising regarding vaccination and education by health care professionals these statistics can be decreased.

Health care professionals, such as physicians and pharmacists are very excited with the first vaccine against a STI. Even though they appreciate the concerns parents and religious groups are expressing, their main focus is decreasing deaths from cervical cancer and reducing the spread of the genital warts from contracting HPV. The main areas of concern for health care professionals is in how to carry out vaccinating all patients, how to ensure that once a patient has received the first vaccine they come back not once but twice more to receive the second and third shots, the side effects the vaccine may cause and the patients who cannot receive the vaccine. If the vaccine is mandated in girls eleven to twelve years old there have been suggestions of administering the first dose when the child comes in for their yearly physical before starting school. The second dose which has to be administered two months after the first dose can be done at the visit when parents come back to get the results of the physical or during the time when many children get sick due to the change in weather. The main concern is how to get parents to take their children back for the third dose, which is six months after the first dose. The only solutions are to have patients called by the nurse and reminded to schedule the visit for the third dose of the vaccine or strongly educate parents as to why all three doses are equally important in ensuring the efficacy of the vaccine. One suggestion that was not widely accepted by the federal and state governments was having the vaccine given directly at school by a nurse to ensure all children would receive all three doses. This would cause the government to have to pay for all vaccines instead of just the ones covered under the VFC program. A second suggestion that would not catch all children in the targeted age group was to have it done
when girls eleven to twelve are admitted into the hospital. Again the problem with this is that they will not be visiting the hospital again when they need their second and third dose. I think the best way to ensure compliancy to the vaccination schedule is through patient/parent education, which will also help with the aforementioned issues of parents. Preclinical trials conducted have not shown any severe side effects. Side effects viewed included pain, swelling, itching and redness at the injection site along with possible fever, nausea and dizziness. These possible side effects can be diminished with proper pre-administration of Benadryl® for the redness and itching, Tylenol® for the possible fever, and an anti-emetic for the nausea. Patients who are not advised to receive the vaccine are those who have an allergy to the vaccine and those who are pregnant. Long-term side effects are not known at this time since the vaccine is so new to the market. I have received the first and second doses of the vaccine so far, my third dose will be in March, and did not experience any side effects whatsoever. Also because the vaccine is so new to the market it cannot be estimated at this time how many females have been vaccinated. Merck claims to have those numbers after the vaccine has been on the market for one full year.

Religious groups have had strong discussions and meetings with Merck, the manufacturer of Gardasil, regarding its use and place in society. Most religious groups feel the vaccine is a good thing in that it will help prevent disease but feel that it should not be mandated in school aged children and abstinence should be the key to decreasing STIs. Religious groups have commented that parents should have the ultimate responsibility in preventing STIs in their children through proper example and responsible teachings. Individuals forget that even though a certain principle or moral value may be taught or enforced in a child, that child will still do what they want to do ultimately. Is it not better to be safe and protect the child from possible viruses that can lead to cervical cancer and genital warts and still at the same time enforce the moral values of the specific religion? I think that due to the severity and epidemic numbers of cervical cancer and genital warts respectively parents have the obligation to vaccinate their child and more importantly continue to educate them. Every state currently has a law allowing parents to decline vaccination on religious grounds without their children being banned from school. This will allow parents to discuss the issue with their religious figure and make an informed decision without feeling pressure from the school boards or fear that their child will be suspended from classes. Senate Bills 1416 and 1417 “require either a vaccine for the HPV or a statement that the parent or guardians have opted out for all girls entering the sixth grade in Michigan’s schools and academics beginning with the 2008 year” Mandating the vaccine is ultimately up to each state after the decision was made by the ACIP to recommend the vaccine. Michigan just recently passed the bills to mandate the vaccine in girls in Michigan from eleven to twelve years old. Religious groups should rest assured that no parent will be forced to act against their beliefs since a law to protect these beliefs is already in place. It should be reinforced that conservatives and religious groups are not against the vaccine in general, only against immunizing females of such a young age.

Whether or not the vaccine Gardasil should be mandated depends on many factors including cost, benefit to risk ratio, and ethical conflicts. We have already established that the vaccine provides benefits such as reducing rates of cervical cancer and genital warts if used before infection of one of the four types of HPV and there is some established benefit against types not contracted if one of the viruses is present. This has a significant impact since “39% of female college students are infected with HPV by 24 months after sexual debut, rising to about 54% by 48 months”. Two studies found a “43-44% cumulative HPV incidence by 36 months in women who were HPV-negative at baseline.” The benefit can only be substantial though if the vaccine is used in the targeted age group of 11-12 ideally, but 9 to 26 theoretically. “HPV prevalence is highest in 14-19 year olds. The percentage of females reporting ever being sexually active by age is 39% for 9th graders, 39% for 10th
The virus does possess the ability to cause potential harms such as reducing the use of cytology screening for cervical cancer due to the belief that screening in no longer needed because of the vaccine. This is a misconception that can be corrected with proper marketing of the drug and patient education by physicians and pharmacists. Health professionals need to remind individuals at yearly check ups and when they administer the three doses of Gardasil that women still need to have pap smears done yearly in order to detect abnormal cytology. Other potential harms resulting from possible actions taken by vaccinated individuals include increased unplanned pregnancies, increased abortions, increased rates of other types of HPV, and increased rates of other STIs including HIV. These increases only hold true if there is in fact an increase in sexual activity once a female has been vaccinated. In older females, it is my opinion that concerned sexually active women would seek out the vaccine and these women are probably the ones who are already practicing safe sex. Therefore I believe there will not be an increase in careless sexual activity and no increases in the aforementioned issues. One of the main reasons why there has been a continued debate about whether the vaccine should be mandatory in order to attend school or not is because past vaccines that have been made mandatory protect the general public health. For example, measles, which is a mandatory vaccine, can be transferred through respiratory secretions and children in a classroom have close contact with each other allowing airborne viruses to be easily transferred. The HPV vaccine differs in the sense that the human papilloma virus is primarily transmitted by sexual contact such as oral sex, genital-to-genital skin contact and intercourse. This can be reduced by lifestyle choices such as abstinence, condom use, and decreased number of sexual partners. Some feel that since the vaccine does not prevent disease in the school setting specifically it should not be required to attend school.

Mandating the vaccine can be discussed in relation to many ethical principles in addition to the scientific principles previously discussed. The first we will address is utilitarianism. “Utilitarianism looks at the rightness or wrongness of a decision based on its consequences.” The consequences of vaccinating individuals are only proven to be the mild side effects such as injection site reaction and nausea, all other harmful possibilities are simply theories and not proven to be significant. Therefore the benefit of vaccinating is a rightful act with no severely negative consequences. “A policy of universal vaccination at age 11-12, when school laws could be more effective than at later stages, could be justified on utilitarian grounds.”

The second ethical principle that relates to mandating the HPV vaccine is the Principle of Double Effect from Natural Law Theory. The Principle of Double Effect is “used to evaluate moral conflicts when an action could produce both good and bad effects.” The HPV vaccine provides multiple benefits such as a reduction in cervical cancer and genital warts. The bad effects include any adverse effects, the possibilities of decreased safe sex practices, an increase in the number of STIs and confusion regarding the screening schedule of cervical cytology. The criteria for the Principle of Double Effect follow: “(1) the action itself must be morally indifferent or good; (2) the bad effect must not be the means by which the good effect is achieved; (3) the motive must be the achievement of the good effect only; (4) the good effect must be at least equivalent in importance to the bad effect.” In regards to the first criteria, it is met since the vaccination is good in that it prevents disease to the recipient and possibly to others in future sexual acts. The second criterion is also met because the possibility of decreased safe sex or confusion about pap smears is not the mechanism by which the vaccine works. These are just possible adverse events related to the vaccine, none of which have been proven significant. The third criterion is also met because the motives of the vaccine are pure in that the only intention is to induce immunity to deadly viruses. The last criteria is also true if and only if the advertising and counseling of the vaccine are done in a way to ensure that sexual responsibility is enforced, timely screening for cervical cancer is educated to the patient and adverse effects are minimized.
"The decrease in cervical cancer and HPV transmission, given that HPV is the most common STI, is likely to outweigh the negatives...the criteria for the Principle of Double Effect will be met."  

The last ethical principle that will be discussed is Principlism. The first addressed will be beneficence which is the act of doing good. This is clear in that the HPV vaccine reduces cervical cancer and genital warts both of which are deadly and epidemic diseases. Non-maleficence involves the potential harms such as decreases in safer sex practices, with resultant increases in STIs, unwanted pregnancy, and abortion. This can be diminished by proper counseling and education. The vaccine is advertised with the reminder that pap smears still need to be done annually and that there are multiple other diseases that are transmitted sexually which the vaccine does not protect against. Justice ensures equal treatment. In regards to economic justice it would have to be ensured that the vaccine was accessible to everyone who needs it. This is accomplished with the addition of Gardasil to the Vaccines for Children (VFC) Program. A second concern with justice is how to make the vaccine available to all uninsured adults. Merck has established a program for adults unable to afford the vaccine again validating the principle of justice. The third concern with justice is the actual mandating of the vaccine. It is not reasonable to force the vaccine upon individuals who plan on life-long abstinence for religious or other reasons. "To force this would violate the principles of justice (and autonomy)." "The principle of autonomy indicates that a person should make their own choices and decisions. It reflects the concept of inherent worth of the individual and to violate it is in essence, to treat someone as less than a person."  In order to keep this principle true the vaccine would have to remain optional to individuals. "To summarize the Principlism approach to HPV vaccine policy, vaccination would clearly be recommended due to beneficence, including at age 11-12 years. However, vaccination would not be required for school or college entry due to autonomy, justice, and hypothetical non-maleficence concerns. HPV vaccination should be covered under the VFC due to justice concerns."  

After review of all the facts and statistics to date, it seems reasonable to assume that other states will follow Michigan’s view on the mandatory vaccination of Gardasil to girls eleven to twelve years of age. Most states also have laws which allow the vaccine not to be given for medical, philosophical or religious reasons so parents will not have to feel forced to have their daughter vaccinated in order to continue attending school. I personally believe that the benefits of Gardasil far outweigh the risks that have been suggested. I have been vaccinated and I would encourage all parents to seek vaccination for their daughter. Teenagers are having sex at younger and younger ages in today’s society and we as health care professionals and parents need to do whatever it takes to eliminate the diseases associated with our children’s poor choices. Mandating Gardasil will help decrease cervical cancer and the spread of genital warts in the future thereby decreasing the health care costs associated with these disease states. With mandating Gardasil though comes the responsibility of ensuring proper education to our young. Parents, pharmacists, and physicians need to encourage children to refrain from having sex until marriage, and if they do choose to have sex that they limit the number of sexual partners they have and practice safe sex methods such as condoms. Physicians also should remind older populations to have regular yearly pap smears in order to detect any abnormal cytology since there are multiple strands of HPV that are not covered by Gardasil and can still lead to cervical cancer and genital warts. Michigan made the correct decision to implement Gardasil as a required vaccination and I hope other states will follow suit.
REFERENCES