

**Editorial**

Dear Reader

*Trachoma is an ocular inflammatory disease, in which the etiologic agent is Chlamydia trachomatis (a bacterium). Trachoma is a neglected disease and an important cause of blindness in the entire world. World Health Organization (WHO) proposes the elimination of trachoma as a cause of blindness by the year 2020. In order to reach this goal, WHO defined the following strategies: surgery for trachomatous trichiasis (TT), antibiotic therapy for active cases, facial hygiene and environmental measures.*

*In this edition, we present an article from one of our regional branches, GVE XIV – Barretos together with the Sanitary Ophthalmology Center/CVE approaching the plan for trachoma elimination. Cities included in Barretos GVE presented detection coefficients varying from 2% to 10%, considering the region endemic and therefore a priority for epidemiologic surveillance. We updated the epidemiologic situation of measles in the State of São Paulo, with two confirmed cases in the GVEs of Santo André and Campinas, with a travel history, and another case in the city of São Paulo, with no history of travelling. With the confirmation of three cases, it is important to reinforce active surveillance for detection and notification of suspected cases, as well as adequate measures for prevention and control, as well as reaching high vaccine coverage rates in the cities.*

*Also in this edition, we start to publish the English version of this Bulletin.*

**Ana Freitas Ribeiro**  
Editor

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## ELIMINATION OF TRACHOMA AS A CAUSE OF BLINDNESS IN THE GVE XIV BARRETOS – STATE OF SAO PAULO

Trachoma is an ocular inflammatory disease affecting the eye conjunctiva and the cornea, caused by ocular infection with *Chlamydia trachomatis* bacterium. The disease has two phases: 1<sup>st</sup> the inflammatory phase, in which the disease is transmittable, and the 2<sup>nd</sup> phase, cicatricial phase, which is non transmittable. Trachoma is an important cause of blindness in the entire world<sup>1</sup>.

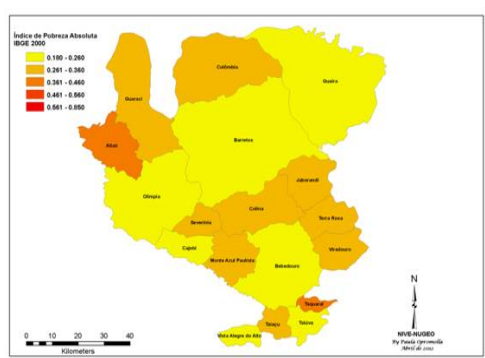
World Health Organization advocates the elimination of trachoma as a cause of blindness by the year 2020. In order to reach this goal, WHO proposes the SAFE strategy, meaning **S** – Surgery for Trachomatous Trichiasis (TT) cases, **A** – antibiotic therapy for infectious trachoma, **F** – Facial cleanliness to reduce transmission and **E** – Environmental improvements.

The Brazilian Health Ministry took into consideration, along with prevalence rates and historic disease foci, the absolute poverty rate of the cities, according to the Brazilian Institute for Geography and Statistics – IBGE – in order to prioritizing cities for the National Elimination Plan. The cities in the Epidemiologic Surveillance Group (GVE) of Barretos are above the baseline level for the poverty criteria of the Health Ministry, defined as 0.47 (Figure 1).

GVE Barretos is located at the northwestern region of the State of São Paulo, 450 kilometers away from the capital of the State; this regional branch presented, in the historic series during the last years, detection coefficients varying from 2% to 10% in different cities, and, therefore, is considered to be an endemic city and, thus, prioritized for trachoma epidemiologic surveillance activities regarding the elimination of the disease as a cause of blindness (Picture 1).

In 2010, the XIV GVE team, in a partnership with the Sanitary Ophthalmic Center of the Epidemiologic Surveillance Center prepared a plan for the elimination of trachoma defining activities for the next five years that took into account all *SAFE* strategy phases.

The objective of this article is to report the actions performed in order to reach the goal of eliminating trachoma as a cause of blindness and report the preliminary results in the cities comprised in the GVE XIV Barretos.



Source: IBGE,2000

**Figure 1** Map of the Regional (GVE XIV), Barretos and the cities comprised, according to the absolute poverty index of IBGE, 2000.

For the “S” component (surgery) of the strategy a training program for monitors in health education and epidemiologic surveillance of trachoma, emphasizing TT was performed, discussing the planning of the activities to be performed. This program trained 38 health professionals of basic health care of the cities in order to allow them to train communitarian health agents and other professionals for the detection and referral of suspected Trichiasis cases of any etiology.

Health professionals of the cities are performing exams designed to identify trichiasis cases in people aged over 50. The goal for adult exams is 80% of this population for the smaller cities. The epidemiologic indicator for achieve elimination certification is less than one case of TT per 1000 inhabitants<sup>3</sup>.

For the “A” component (antibiotics) two approaches will be used: for cities in which the children population is less than 2000 children in the age bracket 1 to 9 years of age, 11 months and 29 days – trachoma census for bigger cities – household enquiries per sample. For the census, the goal for ocular exams in children aged 1 to 9 years old is 98%.

**Picture 1** – Cities comprised by the GVE XIV Barretos according to total population, population aged 1 to 9 years old and older than 15 years of age, trachoma prevalence in the historic series of 2000 to 2011, absolute poverty index and proposal of the activity that must be performed in order to achieve elimination certification for trachoma as a cause of blindness.

CITY	Population	Pop. 1-9 years	Pop. > 15 years	Trachoma prevalence in the historic series	Absolute Poverty Index	Activity to be performed
Barretos	112.101	12.457	90.041	1,0	0,18	Inquiry
Vista Alegre do Alto	6.886	804	5.461	1,0	0,19	Cense
Olímpia	50.024	5.719	40.182	7,9	0,20	Inquiry
Bebedouro	75.035	8.404	59.900	10,7	0,22	Inquiry
Taiúva	5.447	549	4.742	10,7	0,23	Inquiry
Guaíra	37.404	4.474	29.550	7,0	0,24	Inquiry
Cajobi	9.768	1.097	7.873	6,3	0,26	Cense
Viradouro	17.297	2.088	13.571	5,0	0,29	Inquiry
Colômbia	5.994	737	4.663	4,5	0,30	Cense
Terra Roxa	8.505	1.090	6.639	4,9	0,30	Cense
Guaraci	9.976	1.290	7.763	4,9	0,31	Cense
Jaborandí	6.592	786	5.242	9,3	0,31	Cense
Monte Azul Paulista	18.931	2.035	15.191	2,6	0,31	Inquiry
Colina	17.371	2.004	13.766	5,9	0,32	Inquiry
Severínia	15.501	2.043	11.847	0,7	0,34	Inquiry
Taiaçú	5.894	692	4.617	10,0	0,34	Cense
Altair	3.815	518	2.923	10,0	0,37	Cense
Taquaral	2.726	336	2.140	3,1	0,41	Cense
<b>Total</b>	<b>409.267</b>	<b>47.123</b>	<b>326.111</b>			

**Source:** IBGE, 2000 e Demographic Cense 2010.

In order to perform the household inquiries, a sample of children in the preconized age bracket will be selected for exams and multiprofessional teams will be trained for field work.

Two household inquiries are planned for the cities of Barretos, Bebedouro, Colina, Guáira, Monte Azul Paulista, Olímpia, Severina e Viradouro.

The cities comprised in the region agreed, in Managerial Collegiate meetings, to adopt the Plan, complying with the actions to be performed. The agreed indicator for the final goal of intervention was: TF prevalence < 5% for children aged 1 to 9 years in all local or communities areas<sup>3</sup>.

Tables 1 and 2 show that nine cities of GVE XIV Barretos reached the goal for trachoma elimination in the component “A”, meaning exams were performed in 98% of the target population and prevalence of active trachoma was less than 5%. Cities that reached the goal were: Altair, Cajobi, Colômbia, Jaborandi, Taiacu, Taiuva, Taquaral, Terra Roxa and Vista Alegre do Alto.

**Table 1** – Number of examined children and detection rate for Trachoma in children ages 1 to 9 years old in the cities comprised by the GVE – XIV Barretos, 2012.

City of Residence	Trachoma census 2012 – Children aged 1 to 9 years 11 months and 29 days				
	Population	Number of Children evaluated	Number of Cases	Detection Rate %	% of Children Evaluated
Altair	518	511	12	2,4	98,7
Guaraci	1.290	745	2	0,3	57,8
Taiacu	692	681	45	6,7	98,4
Taiúva	549	554	25	4,5	100,9
Taquaral	336	337	12	3,5	100,3
<b>Total</b>	<b>3.385</b>	<b>2.828</b>	<b>96</b>	<b>3,4</b>	<b>84,0</b>

**Source:** data from the Epidemiologic Surveillance System epidemiológica, CVE, 2012

**Table 2** – Number of examined children and detection rate for Trachoma in children aged 1 to 9 years in the cities comprised by the GVE - XIV Barretos, 2013.

City of Residence	Trachoma census 2013 – Children aged 1 to 9 Years 11 Months and 29 Days				
	Population	Number of children evaluated	Number of Cases	Detecton Rate %	Percentage of evaluated Children
Taiacu	718	718	8	1,1	100,0
Cajobi	1.097	1.088	4	0,4	99,1
Jaborandi	786	780	31	3,9	99,2
Colômbia	737	739	5	0,7	100,2
Terra Roxa	1090	1070	6	0,6	98,2
Vista Alegre do Alto	804	804	0	0,0	100,0
<b>Total</b>	<b>5.232</b>	<b>5.199</b>	<b>54</b>	<b>1,0</b>	<b>99,4</b>

**Source:** data from the Epidemiologic Surveillance System, CVE,2013.

During the year 2012 the city of Taiacu although reaching the goal for the number of examined children did not reach the elimination target. The city only reached the elimination goal in the year 2013. The city of Guaraci maintains active search actions in order to reach the goal proposed by WHO.

We emphasize that, prior to active search activities, health education actions are performed for all schools and day care centers, informing about the disease and on how to prevent, treat and control cases.

Detected cases were notified in the Notifiable Disease Information system (SINAN-NET – Trachoma enquiry). All trachoma cases and their contacts were treated with systemic Azithromycine according to the scheme preconized by the Health Ministry. Cases are under follow up until cure. Household contacts of confirmed cases were evaluated and treated<sup>4,5</sup>.

The cities of Altair and Colina reached the goal to evaluate 80% of the population aged 50 or more years old for trichiasis detection. Up to now, no confirmed cases of trichiasis were identified. Table 3 shows preliminary data.

**Table 3** – Partial data of the Trachomatous Trichiasis cases in the cities comprised by the GVE XIV Barretos, during the years 2012 and 2013.

City of Residence	Population aged 5 years or older	Goal of 80% exams	Total Evaluatede	Percentage Performed
Altair	733	587	677	92,4
Cajobi	2.448	1.959	1.380	56,4
Colina	4.167	3.334	3.742	89,8
Colômbia	1.266	1.013	844	66,7
Monte Azul Paulista	4.772	3.818	83	2,2
Olimpia	13.038	10.431	1.093	8,4
Severinia	2.973	2.379	1.639	55,1
Taquaral	693	555	380	68,5
Terra Roxa	2.035	1.628	736	36,2
Viradouro	4.021	3.217	2.130	54,0
<b>Total GVE XIV</b>	<b>36.146</b>	<b>28.921</b>	<b>12.704</b>	<b>43,9</b>

**Source:** data from the Epidemiologic Surveillance System, CVE

## CONCLUSIONS

The actions performed in these cities were started after agreement in Regional Managerial Collegiates (North and South), according to the Blinding Trachoma Elimination Plan, designed by GVE XIV Barretos in collaboration with the Sanitary Ophthalmology Division, based on the activities of epidemiologic surveillance for Trachoma elimination, such as triage, case detection, case treatment and follow up, epidemiologic situation follow up and notification to the SINANS-NET, as well as health education activities and investigation of contacts.

Trachoma elimination plan for GVVE XIV Barretos includes the performance of censuses in the smaller cities and enquiries for household samples. This is a partial result of these activities.

Activities are ongoing in order to reach the goal proposed by WHO, and include the technicians from GVE XIV Barretos and professional of health care teams in this collaborative work.

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## UPDATE

### MEASLES IN THE STATE OF SÃO PAULO, 2014

Measles is a highly contagious disease and virtually all susceptible persons acquire the disease after exposed to a case. Transmission may occur by the dispersion of droplets containing viral particles in the air, especially in closed environments such as day care centers, schools, health care facilities and means of transportation, including airplanes. The virus may be transmitted five days before and five days after cutaneous eruption.

The triple viral vaccine is the safest and most efficient preventive measure against measles, protecting also against rubella and mumps.

Travelers and people attending mass events must keep their vaccination schedules up to date, before travelling or before attending the event (preferably 15 days before).

In 2014, by the 10<sup>th</sup> Epidemiologic Week (SE) (ending in March, 8<sup>th</sup>, 2014), Brazil presents 136 confirmed cases of measles, 119 of which in Ceará, where circa 44% of the cases occurred in children under one year old; other 11 cases were registered in Pernambuco and six cases in São Paulo, Laboratory investigation identified the genotype D8 related to the current cases of the three States, present in almost all of the 211 cases of the disease registered in Brazil in 2013. Date of the exantema of the last confirmed case in Brazil, to date, occurred in Epidemiologic Week (EW) 10/2014.

#### Measles – Epidemiologic situation in March, 2014, State of São Paulo

In 2014, up to EW 10, six measles cases were confirmed in the State of São Paulo (ESP) in the GVE – Santo André (1 case), CVE – Campinas (1 case) and in the city of São Paulo (MSP) (4 cases: 1 isolated case and 3 cases in a family cluster).

Cases registered in GVE – Santo André and GVE – Campinas related recent travel history (to the Southeast Asia and Ceará, respectively). There is no report of travel or external source of infection for the four cases registered in MSP. Three of the cases (MSP) required hospitalization and there were no deaths.

Age brackets stricken were 8 months old, 1 year old, 3 years old, 9 years old, 21 and 34 years of age. None of the stricken had documented registers of vaccine (TV or DV).

In five of the cases, processing of clinical samples resulted in positive RT-PCR for measles and sequencing processed at IAL and Fiocruz identified the genotype D8, in circulation since 2012 in European and Asian countries and, since 2013, in Brazil. In one case, there was increase of IgG in the pairing of the samples.

Exanthema date of the last confirmed case in the State of São Paulo, up to March, 19<sup>th</sup>, 2014, is February, 17<sup>th</sup>, 2014.



Therefore, the ALERT is maintained for all health professionals shall consider the suspicion of measles, when facing cases of fever and exanthema.

Quick detection of cases and timely notification allow quick answer to any virus introduction, with the due start of control measures designed to interrupt and minimize circulation and transmission.

Recommendation to Regional and Municipal Surveillance Branches:

Branches must issue an alert to all public health facilities and especially, for private facilities (health unities of low, medium and high complexity), employing all possible media, about the national epidemiologic situation of measles, so that health professionals pay special attention to all suspected cases of exanthematic disease. These cases must be immediately notified and investigated to evaluate if they are suspected cases of measles (and/or rubella).

In the detection of suspected cases, Municipal secretaries must:

- Immediately (deadline: 24hs) notify the case to the State Secretary of Health;
- Perform blood collection (sera) for laboratory diagnosis (serology);
- Adopt control measures (selective vaccine blockage of suspected cases that must be broadened when serology is reactive);
- Recommend social isolation.

**Important recommendations:**

- Alert travelers and mass events participants about the need to assure their vaccine schedules are updated before travelling or attending the event (preferably 15 days before).
- Recommend the MMR vaccine with special attention to travelers that are going to the Northeast region of the country, including children aged six months to one year of age. The dose administered at this age bracket will not be considered valid for the vaccine scheduled adopted by the State, and administration of SRC at 12 months of age and tetravalent (MMRV) at 15 months of age.
- Reinforce vaccination for professionals working in tourism, employees of air travel companies, workers of inland transit, taxi drivers, employees of hotels and restaurants and other professionals who maintain contact with travelers.
- Evaluate and update whenever needed vaccine situation for the different age brackets, including people participating and volunteers (FIFA World Cup Brazil 2014™) of mass events.
- Reinforce vaccination of health professionals (physicians, nurses, dentists and others) and education professionals.
- Reinforce the evaluation of vaccine coverage and homogeneity of the routine vaccination for the different age groups, including people participating or volunteering in mass events (FIFA World Cup Brazil 2014™).
- Reinforce vaccination of health professionals (physicians, nurses, dentists and others) and education professionals.
- Reinforce collaboration between public and private sectors (NHE, CCIH, laboratories) in order to allow uniform notification as well as increasing awareness regarding the



importance of correct and opportune notification for the start of control measures, reinforcing the occurrence of mass events.

- Recall of the samples presenting REACTIVE EgM for measles or rubella in public/private sectors, forwarding them to the laboratory of reference in the State of São Paulo: Department of Respiratory Diseases, Virology Center of the Instituto Adolfo Lutz, for laboratory confirmation.
- In strongly suggestive suspected cases of measles or rubella, or when Reactive IgM are presented, collect clinical samples (heparinized blood , nasal and pharyngeal secretions and urine), for viral isolation and sequencing.
- In the presence of a case with Reactive IgM or indeterminate for measles or rubella, collection of a second blood sample (sera) is indispensable, at least 15 days after the 1<sup>st</sup> sample collection for IgG pairing.
- Update health professionals for exanthematic febrile diseases, conduct at first attention, diagnostic confirmation of cases and starting control measures.
- Identifying possible transmission areas: at the moment a suspected measles case is notified, perform ACTIVE SEARCH for detection of other possible cases (health services, public network laboratories, etc.)

#### **Reinforce an important guideline for the population:**

Whenever fever and exanthema are presented, avoid contact with other persons until evaluation by a health professional and look immediately for health services.

#### **All suspected cases of measles and rubella must be notified to:**

- Municipal Health Secretary an/or to
- Central Surveillance/CIEVS/CVE/CCD/SES-SP, at the telephone 0800 555 466 (working nonstop everyday)
- Online notification: [www.cve.saude.sp.gov.br](http://www.cve.saude.sp.gov.br)
- And/or by the e-mails: [notifica@saude.sp.gov.br](mailto:notifica@saude.sp.gov.br) or [dvresp@saude.sp.gov.br](mailto:dvresp@saude.sp.gov.br)

*This document was elaborated and updated by the Technical Staff of the Respiratory Transmitted Diseases Division/CVE/CCD/SES-SP, with the collaboration of the Immunization Division/CVE and the Virology Center of the Instituto Adolfo Lutz, in March, 2014, São Paulo, Brazil.*

## TECHNICAL REPORT

### VACCINE AGAINST HUMAN PAPILLOMAVIRUS (HPV)

#### 1. HPV virus

HPV virus (an acronym for Human Papillomavirus) is associated to the presence of many different types of cancer, especially among women. It is a virus able to cause skin or mucosa lesions that, in general, resolve by the action of the immune system<sup>1</sup>.

The virus is highly contagious, and contamination may occur after a single exposition. HPV transmission occurs by direct contact of infected skin or mucosa and the major form is by sexual transmission. Mother to baby transmission may also occur during pregnancy and deliverance (vertical transmission). It is estimated that circa 25% to 50% of the female population and 50% of the males in the world are infected by the HPV virus<sup>2</sup>.

Most of HPV infections is transitory, and the immune system is able to solve them, receding between six months to two years. It is estimated that only 10% of the infected persons will present any clinical manifestation such as precursor lesions of cervical cancer and genital warts. The period required for the appearance of the first clinical manifestations varies from 2 to 8 months typically, but may take up to 20 years<sup>3</sup>.

More than 150 different types of HPV have already been described, of which 40 to 50 types may infect anal genital region in males and females and are divided into two important groups<sup>4</sup>.

- High oncogenic risk (for instance types 16 and 18) associated to genital cancer such as cervical cancer.
- Low oncogenic risk (for instance types 6 and 11), associated to benign lesions such as genital warts.

Oncogenic HPV virus penetrated the cell triggering a series of alteration in its functions. Altered cells start to produce new strains of the virus and, at the change time, changes in their interior (atypia), which slowly evolve until turning into carcinogenic cells (this is a slow transformation that takes from 10 to 15 years)<sup>3</sup>.

Cervical cancer is a serious disease that may threaten women's' lives. Initially asymptomatic, the infection by HPV may evolve to a precursor lesion for cancer and, if left untreated, these lesions evolve, in some years, for cervical cancer, with symptoms like vaginal bleeding, vaginal discharge and pain.

Circa half of all the women diagnosed with cervical cancer are aged between 35 and 55 years and were probably exposed to HPV during their adolescence, in general by sexual relationships with infected partners.

Data from the World Health Organization show that every year, in the world, 500 thousand women are diagnosed with the disease. Among these, 270.000, more than half of them, will die. In Brazil, according to the National Cancer Institute (INCA) the number of new cases estimated for 2014 is 15.590. In 2011, 5.160 women died of cervical cancer<sup>5,6</sup>.

HPV viruses of types 16 and 18 (high risk) account for up to 90% of the cases of rectal cancer, 60% of vaginal cancers and up to 50% of vulva cancers. Types 6 and 11 (low risk)

may account for recurrent respiratory papillomatosis of the child, a rare benign tumor affecting the larynx but that may extend to the entire respiratory tract, with important pulmonary complications. The child may be contaminated at the moment of vaginal deliverance, if the mother is infected.

HPV vaccine is an important strategy for the reduction of cancer cases in women. Cervical cancer is the fourth death cause by cancer among Brazilian women. The first is breast cancer, followed by tracheal cancer, bronchial cancer and the third colon and the rectus<sup>6</sup>.

It is important to remind that, despite the infection by high risk types (16 and 18) being frequent among women, the occurrence of cervical cancer is low. Conditions such as precocious start of sexual life, high number of sexual partners, prolonged use of hormonal contraceptives, multiple births, tobacco use, genetic and immunological factors increase the risk for the progression of the infection by HPV to cervical cancer.

Due to the fact that persons infected by HPV in general do not present any symptoms, many of them ignore to be carriers of the virus. Most of the women discover they have HPV when receiving an abnormal Papanicolaou results.

Cervical and vaginal smears, known as Papanicolaou exam, help the detection of abnormal cells in the lining of the cervix, allowing treatment before the onset of cancer.

Papanicolaou allows the identification of cell alterations in the cervix but do not detect the presence of the virus. However, is the best method for detection of precursor lesions and cervical cancer. According to the guidelines established by the Ministry of Health, the exam must be made, preferably, by women aged between 25 to 64 years who are or have been sexually active. The first two exams must be made with the interval of one year between each other and, if results are normal, the exam may be performed every three years<sup>7</sup>.

Diagnosis of genital warts may be made by clinical exam.

### **1. The role of the HPV vaccine in the prevention of cervical cancer.**

HPV vaccine is tetravalent, since it combines four types of HPV. Avoids the infection and, therefore, cervical cancer cases caused by types 16 and 18 and genital warts caused by types 6 and 11. HPV vaccine has been introduced in more than 51 countries as a public health strategy.

There are evidences that the vaccine gives higher protection and indication for persons who have never had contact with the virus, inducing tenfold more antibody production than the natural infection produced by HPV<sup>8</sup>.

Vaccine is exclusively intended for prevention and has no proven effect in pre existent infections or in the disease already established. To the moment, there is no scientific evidence of statistically significant benefits of vaccinating women who were previously exposed to HPV.

It is important to remind that the vaccine is a primary prevention tool and does not substitute the tracking of cervical cancer (Papanicolaou), since the vaccine gives no protection against other sexually transmittable diseases such as HIV, syphilis, hepatitis B and C and, therefore, it is important to use preservatives in all sexual relationships.

Particular attention is drawn to the fact that, despite the correct use of preservatives effectively reduces the infection by HPV, the risk of contamination exists, especially by types

6 and 11 – accountable for circa 90% of vaginal warts cases – in case these lesions are located in areas unprotected by the preservatives.

## 2. The vaccine that will be used in Brazil

To date, two vaccines against HPV have been developed and registered. The Ministry of Health opted for the tetravalent vaccine that will be used in the vaccination actions in the country<sup>9,10</sup>.

<p>Vacina Quadrivalente Recombinante (Laboratório MSD, Gardasil®)</p>	<p>Vacina Bivalente (Laboratório GSK, Cervarix®)</p>
<ul style="list-style-type: none"> <li>• Confere proteção contra HPV tipos:               <ul style="list-style-type: none"> <li>• 6</li> <li>• 11</li> <li>• 16</li> <li>• 18</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Confere proteção contra HPV tipos:               <ul style="list-style-type: none"> <li>• 16</li> <li>• 18</li> </ul> </li> </ul>

Tetravalent recombinant vaccine gives protection against HPV types 6, 11, 16 and 18 (Gardasil ®) and bivalent vaccine gives protection against HPV types 16 and 18 (Vervarix ®).

Tetravalent vaccine, produced by the Merck, Sharp & Dohme Laboratory (MSD) is approved, in Brazil, for prevention of pre-cancerous genital lesions in the cervix related to HPVs 16 and 18 and also for the prevention of genital warts in women and men, related to HPV 6 and 11.

Bivalent vaccine, produced by the GlaxoSmithKline Laboratory (GSK) is approved for the prevention of genital pre-cancerous lesions of the cervix in women, related to HPV 16 and 18.

According to the registration in the National Sanitary Surveillance Agency (ANVISA), these vaccines are indicated to distinct age groups. The tetravalent vaccine is indicated to women and men aged between 9 and 26 years, and bivalent vaccine is indicated to girls 9 years of age and older, with no age restriction.

The Ministry of Health opted for the tetravalent vaccine against HPV virus, that protects against oncogenic serotypes 16 and 18 and serotypes 6 and 11, associated to genital warts.

## 3. Studies on Immunogenicity, efficacy and duration of the protection

It was possible to observe that almost 100% of the women vaccinated with the tetravalent vaccine presented seroconversion after completing the vaccine scheme (0, 1-2 and 6 months), for the four types of HPV, one month after the third dose. Antibody titers after vaccination are higher when compared to the rates reached after natural infection<sup>3</sup>.

To date, there is no correlate of antibody and protection titers, however efficacy studies evaluated outcomes, that is, if after vaccination with the complete scheme, vaccinated women presented precursor lesions for cancer and genital warts.

Circa 20.000 women aged between 16 and 26 years participated in the first studies on the efficacy of tetravalent vaccine. Efficacy of tetravalent vaccine for the prevention of cervical cancer reached 98% (CI 95%, 86-100) and 100% (CI 95%, 94-100) for genital warts<sup>11,12,13</sup>.

Studies on tetravalent vaccine showed broadened protection for other serotypes related to types 16 and 18, such as types 31, 33 and 45. However, existing studies have not yet been able to determinate the clinical relevance and the duration of the protection<sup>14</sup>.

Results of follow up studies with tetravalent vaccine have show that elevated protection and elevated antibody titers last for at least nine years<sup>15,16</sup>.

#### **4. Characteristics of HPV vaccine**

HPV virus has a capsule constituted by two proteins called L1 and L2. It was possible to observe that, after natural infection by the HPV formation of neutralizing antibodies against L1 occurs and, from these results, HPV vaccines were developed.

Traditional methods for vaccine development, such as inactivation or attenuation, did not work for the production of HPV vaccine. In 1990, it was seen that L1 and L2 proteins, obtained by genetic recombination, were organized in a structure similar to the viral capsule, then called VLP (virus-like particles).

Viral capsules are unable to replicate. HPV vaccine is an inactivated product, highly immunogenic, able to induce high antibody titers, superior to levels obtained by natural infection with no risk of causing the disease<sup>8,17</sup>.

#### **5. Objective of the vaccination and goals**

The major objective of the vaccination against HPV in Brazil is to prevent cervical cancer, reflecting in the reduction of incidence and mortality caused by this disease. Taking into account that the tetravalent vaccine will be used, with serotypes 6, 11, 16 and 18, we will also obtain prevention of genital warts<sup>9,10</sup>.

Population to be vaccinated will be adolescents aged 9 to 13 years, distributed as follows:

- In 2014: girls aged 11, 12 and 13 years;
- In 2015: girls aged 9, 10 and 11 years;
- From 2016 onwards: Nine year old girls.

The goal is to vaccinate 0% of the target population, representing, in Brazil, 4,16 million adolescents and, in the State of São Paulo, 808.318. The aim is to reach high vaccine coverages and, thus, reduce the transmission of HPV virus even among unvaccinated persons (herd immunity).

Boys will not be included in vaccination actions, since studies show they are indirectly protected with female vaccination, reducing the transmission of HPV virus types related to genital warts<sup>18</sup>.

#### **6. HPV vaccine, presentation, dose and composition**

HPV vaccine is presented as injectable suspension, single dose, in a package containing 10 ampoules. Each dose is 0,5 ml.

**Figure 1.** Composition of HPV vaccine.

20 microgramas Proteína L1<sup>2,3</sup> do Papilomavírus Humano<sup>1</sup> Tipo 6  
 40 microgramas Proteína L1<sup>2,3</sup> do Papilomavírus Humano<sup>1</sup> Tipo 11  
 40 microgramas Proteína L1<sup>2,3</sup> do Papilomavírus Humano<sup>1</sup> Tipo 16  
 20 microgramas Proteína L1<sup>2,3</sup> do Papilomavírus Humano<sup>1</sup> Tipo 18

Excipientes: adjuvante sulfato de hidroxifosfato de alumínio amorfo (225 microgramas de Al), cloreto de sódio, L-histidina, polissorbato 80, borato de sódio e água para injetáveis

<sup>1</sup> HPV Human papilloma virus

<sup>2</sup> Protein L1 in the form of virus like particles produced in yeast cells (*Saccharomyces cerevisiae* CANADE 3C-5 (Strain1895)) by recombining DNA technology.

<sup>3</sup> Adsorbed in the amorphous adjuvant of hidroxifosphate aluminium sulphate (225 micrograms Al).

Source: Brazil, 2013

## 7. Administration via and conservation

HPV vaccine must be maintained in temperatures between +2° C and +8° C, administered intramuscularly in the deltoid. The vaccine must not be frozen.

## 8. Vaccination scheme

The vaccination scheme initially indicated and adopted in many countries is three doses, applied in intervals of 0, 1-2 and 6 months apart. In this scheme, the interval between the first and the second dose is one to two months (minimum 30 days); second and third doses shall be applied in a four month interval (120 days) and the first and the third dose must observe a six month interval between them (180 days).

In Brazil, the Ministry of Health will adopt the extended vaccination scheme, applying three doses at 0, 6 and 60 months, resulting in a six month interval between the first and the second dose and a six month interval between the first and the last dose, at 60 months.

There are studies already published on immunogenicity with two doses (six month interval) of the tetravalent vaccine in comparison with three dose scheme (0, 2 and 6), showing that antibody titers were not inferior, registering even higher titers in the first group. Third dose 5 years after the first is an additional warranty for the maintenance of a longer answer<sup>19,20,21</sup>.

This decision was made after recommendation of the Technical Advisory Committee of the Pan-American Health Organization (TAG/OPA) and, after approved by the Technical Immunizations Committee of the National Immunization Program of Brazil (PIN), acknowledging the need for additional data at long term (Brazil, 2013).

Published studies show the vaccine response after the extended scheme is not inferior to the scheme 0, 1-2 and 6 months<sup>19,20,21</sup>.

This decision was made after the recommendation issued by the Technical Advisor Committee on Immunizations of the Pan-American Health Organization (TAG/PAHO) and after approval by the Technical Committee for Immunizations of the National Immunization Program of Brazil (PNI).

Results from a study on immunogenicity with two doses (at a six month interval) of the tetravalent vaccine in the group of girls aged 9 to 13 years, in comparison with three doses

(0, 2 and 6) in the group of young women aged 16 to 26 years did not result in inferior levels, resulting even in higher antibody titers in the first group<sup>18</sup>.

Neuzil et. al. observed that the higher the interval between the two first doses of the tetravalent vaccine the higher the antibody titers obtained immediately after the third dose, which may result in a more robust immunologic response in adolescents and young adults<sup>21</sup>.

The extended scheme was already adopted by countries like Canada (Quebec and British Columbia), Mexico, Colombia, Chile and Switzerland<sup>22</sup>.

#### **ATTENTION!**

- *vaccine scheme to be employed in Brazil will be three doses (0, 6 and 60 months), meaning the interval between the first and the second dose will be six months and between the first and the third will be 60 months;*
- *in situations in which delays occur between the doses, there will be no need to start the vaccine scheme over;*
- *It is recommended for adolescents who started the scheme with the bivalent vaccine,, that the same vaccine must be employed to finish the scheme, in the same services in which they started their schedule. However, if this is not possible, they may finish the scheme with the tetravalent vaccine in public health services;*
- *when the vaccine previously administered is unknown, the adolescent may finish the vaccine scheme with the tetravalent vaccine in public health services;*
- *when the number of doses already administered is unknown, start the scheme with the tetravalent vaccine;*
- *there are no available data on immunogenicity or efficacy of both HPV vaccines when used in interchangeable administration. Therefore, apply the same vaccine whenever possible;*
- *adolescents who completed the three dose scheme in private clinics will not be reveaccinated with the tetravalent vaccine;*
- *adolescents who received two doses of HPV vaccine in private clinics who no longer can complete the scheme in the same place, must receive the third dose 6 months after the first.*

#### **10. Population to be vaccinated**

Target population of the vaccine is female adolescents.

In the year the vaccine (2014), adolescents aged 11, 12 and 13 years will be vaccinated. In 2015, vaccine will be offered to adolescents aged 9, 10 and 11 years and, from 2016 forwards, 9 year old adolescents will be vaccinated, as will be shown in the figure below.

Indian populations are a group in higher vulnerability for diseases. Target population for the vaccine comprises female Indians aged 9 to 13 years in the introduction of the vaccine (2014) and 9 year olds from the second year forwards (2015).



**Figura 2:** Distribution of age brackets of the target population receiving HPV vaccine.

Year	Target population
2014	Female adolescents aged 11, 12 and 13 years, 11 months and 29 days. Female Indians aged 9 to 13 years, 11 months and 29 days.
2015	Female adolescents aged 9, 10 and 11 years, 11 months and 29 days. Female Indians aged 9 years, 11 months and 29 days.
2016 forward	Female 9 year old adolescents and during the year girls complete 9 years of age. Female 9 year old Indians.

Source: Brazil, 2013.

### 11. Simultaneous administration with other vaccines

HPV vaccine may be simultaneously administered with other vaccines included in the vaccine Schedule.

#### **Attention!**

*Whenever possible, profit from HPV vaccination to update vaccination scheme for dT (diphtheria and tetanus), hepatitis B vaccine, MMR (measles, mumps and rubella) and yellow fever.*

*It is important to remind that simultaneous vaccination is not indicated for yellow fever vaccine and MMP, except in risk situations*

### 12. Contraindications

Contraindications for HPV vaccine are<sup>23</sup>:

- Anaphylactic\*\* reaction to vaccine components;
- Anaphylactic reaction caused by a previous dose;
- Pregnant women, since there are no conclusive studies until the moment. If the adolescent becomes pregnant after the start of the vaccine scheme, following doses must be deferred until post partum. In case the vaccine is administered during pregnancy, no additional intervention is required, only the adequate prenatal follow up.

It is important to remind that studies on HPV vaccine performed in women who became pregnant while receiving the vaccine scheme, vaccination was interrupted and the required doses were administered after deliverance. These pregnant women were followed up and there was no observed increase in the rate of abortions or congenital malformations<sup>8,23,24,25</sup>. There were also no observed adverse events associated to the vaccine in vaccinated women who were breastfeeding<sup>8,22</sup>.

### 13. Precautions

Below we list some situations that require attention previously to vaccination:

- Severe acute febrile disease: in severe acute febrile disease it is recommended to postpone the vaccination, especially in order to avoid confusion of these symptoms with possible vaccine events. Adolescents suffering a cold may be vaccinated.
- Thrombocytopenia: the vaccine must be administered with precautions for girls with thrombocytopenia (reduction in the number of plaquettes) or any other coagulation

disturbance, due to the risk of occurrence of bleeding or hematomas after intramuscular injection.

- Immunosuppressed: the adolescent may be vaccinated.
- Breastfeeding: the adolescent may be vaccinated

#### 14. Post vaccination adverse events (EAPV)

HPV vaccine is safe and well tolerated, but, as may happen with any other vaccine, may present adverse events, as described in the figure below:

**Figure 3:** Adverse events aftger HPV vaccine

Type of adverse event	Major signs and symptoms
Local reactions	Pain, swelling and moderate erythema, in the application site.
Systemic manifestations	Headache; 38° C Fever or higher; Syncope (fainting).

Source: Brazil, 2013.

Syncope is a transitory consciousness alteration, accompanied by loss of conscience and posture tonus, caused by the diminishing of the blood flow to the brain, with spontaneous recovery, most of them occurring during the first 15 minutes after vaccination. It is one of the most common causes of the partial or total consciousness loss and, despite being a benign disturbance, in general with good evolution, has the potential to produce lesions such as hip or limb fractures<sup>1</sup>.

In Australia and in the United States, where the HPV vaccine is already administered, syncope rate is low, of 8,0/100.000 distributed doses<sup>26,27</sup>.

There is, in general, a striking stimulus such as intense pain, expectation of pain or sudden emotional shock. Diverse different factors, such as prolonged fasting, fear of the injection, hot or crowded environments, girls remaining standing on their feet for a long time, may increase the occurrence of syncope<sup>9</sup>.

Therefore, in order to reduce the risk of falls and allow immediate intervention in case syncope occurs, the adolescent must remain seated and under observation for circa 15 minutes after administration of HPV vaccine.

#### **Attention!**

*Adolescents who presented syncope may complete the vaccine scheme .*

In the United States, during the period comprised between June, 2006 and March, 2013, circa 56 million doses of HPV vaccine were distributed and there was no observed increase in the occurrence of Guillain-Barré Syndrome and convulsions<sup>28</sup>.

Despite many studies and universal use of the HPV vaccine, the investigation of EAPV is indispensable for evaluation of the product safety. Therefore, notification and investigation of serious adverse events must be performed. In the occurrence of syncope, notification must be made in up to 24 hours<sup>29</sup>.

As preconized for other vaccines, in the occurrence of the situations described below, in order to avoid any undue association to the vaccine, notification must also be made in up to 24 hours<sup>29</sup>.

- Hospitalization during 24 hours;
- Significant dysfunction or incapacity (sequelae)
- Risk of death;
- Death.

### **15. Implementation of HPV vaccine implantation**

In order to achieve success in the vaccination campaign against HPV, integrated work between State Secretaries, Municipal Secretaries, Regional Health branches, Basic Health Unities and public and private schools is fundamental. Therefore, it is important that responsibilities and actions be well defined and established, as well as an activities chronogram.

Partnership with schools, requiring the involvement of teachers in the awareness of the importance of HPV vaccine is fundamental, contributing to the issuing of information, acceptance and participation of the adolescents in the vaccination.

HPV vaccine may be administered in the schools or in the health unities, depending on the local reality.

It is important to make clear that access of the adolescents to health services, including vaccination, even with no authorization or unaccompanied by parents or responsible, is a right previewed by the Brazilian Federal Constitution, by the Child and Adolescent Statute (Law 8069/1990) and the Unified Health System (Law 8080/1990).

We suggest, below, some actions for the implantation of the HPV vaccine in the public network:

- Establishing a Mobilization Committee articulating the Basic Health staff, women's and adolescents' health staff, SDT-Aids teams, Department of Education, Indians' health staff, Welfare departments (for vaccination actions designed for adolescent living in the streets and non enrolled in schools);
- Performing regional and local seminars to raise awareness and issue guidelines for health and education professionals regarding the importance of the vaccination;
- Vaccination offered at the schools: this is a very important action to reach the proposed goal of 80% vaccine coverage of adolescents. The experience of the more than 50 countries already using HPV vaccine shows that better vaccine coverages may be obtained with vaccination at schools, since this strategy makes access to the vaccine easier for adolescents who do not seek or have difficulties to access health unities. Even more, as opinion makers, schools are legitimate to disseminate health information to adolescents<sup>9,10</sup>.
- Define which schools will be under responsibility of each health unit;

- Visit the schools in order to define meetings discussing the vaccination;
- Schedule meetings with the management of the schools, their coordination, teachers (especially teachers of sciences and biology), parents and persons in charge of the children to raise awareness regarding the importance of the vaccination and of the strict compliance to the vaccine scheme, with three doses;
- It is important to make clear that vaccination of the adolescents in the schools may happen without any authorization or when they are not accompanied by parents or people in charge of them. In case parents or people in charge of adolescents do not authorize their vaccination, they must present the Term of Refusal.

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## NOTIFIABLE DISEASES AND DISORDERS

**Table 1** – Confirmed cases and Outbreaks of diseases and disorders notified to the CVC, State of São Paulo, from 2011/2012\*/2013\*, July to September and October, November and December, 2013\*

Diseases/Disorders	2011	2012*	2013*	2014*
				Jan.
<b>CONFIRMED CASES</b>				
Accidental Tetanus	27	21	25	2
Acute Flaccid Paralysis (for < 15 years)	91	88	74	11
American tegumentar leishmania	266	312	281	15
Botulism	0	5	0	2
Brazilian Spotted Fever/Rickettsioses	80	82	58	0
Cholera	1††	0	0	0
Congenit Rubella Syndroma	0	0	0	0
Conjuntivitis§§	1.187.356	318.394	186.464	8.615
Creutzfeldt-Jacob disease and Other Prionic diseases	17	40	38***	5*
Dengue (Autoctonous and imported cases)	97.882	25.383	209.052	2.165
Diarrhea (Cases under follow up by the MDDA)**	940.200	1.146.212	1.041.743***	111.638
Diarrhea (Casses involved in outbreaks)	9.524	5.675	1.367***	368
Domestic/sexual and/or other kinds of violence (excluding urban violence)	31.408	44.205*	37.887	=
Haemolitic Uremic Syndrome	1	1	3	0
Hantavirus	21	12	13	0
Hepatitis A (Casos esporádicos)	204	175	231	14
Hepatitis A (Casos envolvidos em Surtos)	61	70	40	3
Hepatitis B	3.964***	4.083***	3.424***	182
Hepatitis B + C (co-morbidade)	141***	135***	113***	4
Hepatitis C	6.442***	6.404***	5.027***	242
Leptospirosis	970	787	898	65
Measles	27	1	5	3
Meningogocccic disease	1.363	1.168	958	59
Mumps [Epidemic Parotitis]	150	215	281	4
Other Meningitis	833	968	799	79
Other Bacterial Meningitis	1.724	1.638	1.413	85
Poliomielitis (wild poliovirus)	0	0	0	0
Rotaviruses (for < 5 years)§	1.522	23	124	6
Rubella	0	0	0	0
SARS/Human Influenza A (H1N1)†	26	371	1.994	8
Schistosomiasis ( Total cases)	1.080	1.094	690	45
Schistosomiasis (Autoctonous cases)	84	85	52	2
Trachoma¶	1.760	2.202	2.481	109
Typhoid Fever	3	2	2	1
Varicella	18.375	18.982	24.799	61
Viral Meningitis	4.230	5.294	4.470	329
Visceral leishmania	228	247	200	16
Whooping cough	914	1.029	1.570	339
<b>CONFIRMED OUTBREAKS</b>				
Conjuntivitis§§	9.041	776	292	95
Diarrhea	137	138	55***	26
Hepatitis A	15	7	8	1
Mumps [Epidemic Parotitis] with no complications	40	88	37	4
Varicella	2.747	3.001	3.641	25

Source: SINAN Net (with corrections)

(\*) 2012, 2013\* and 2014\*- preliminary data- (\*\*) Source: SIVEP\_DDA/SVS/DATASUS - (\*\*\*) data update

(†) Source: SINAN Web (with corrections) – SARS Severe Acute Respiratory Syndrome Hospitalized cases – data starts at April, 2009

††) Imported case - Acum.(accumulated cases)

(§)Source: Sentinel Surveillance for Rotaviruses and SINAN Net (with corrections - (§§) Sinan Net outbreak and conjuntivitis surveillance system

(¶)Source: Trachoma Inquiry /SINAN Net (...) = unavailable data due to different deadlines for data closing.



## PROTECTION NETWORK: ESSENTIAL CONNECTIONS FOR HUMAN RIGHTS AND PEACE CULTURE PROMOTION



Violence and accidents, classified in the International Disease Classification as external causes, are acknowledged as important disorders for health surveillance purposes. In the region (CGR Alto Vale do Paraíba), during the period from 2009 to 2011, these causes represent the fourth death cause. Among external causes, accidents are the major death cause, followed by homicides, striking especially men aged 15 to 49 years, since they are more prone to urban violence<sup>1</sup>. According to data from the IBGE (Brazilian Institute of Geography and Statistics), mortality due to external causes influences the population profile, since in Brazil more males are born than females, but the proportion changes: more women reach old age than males.

Mortality is a factor signaling the importance of this health disorder, despite this, occurrences of death are insufficient to give the adequate dimensions of the problem, since there are situations that do not lead to death and do not demand medical attention and, therefore, are not recognized as a consequence of violence situations. Thus, there is the need to broaden the glaze on data collection in order to identify causes and groups more stricken by them, in order to subsidize interventions and public policies.

In 2009, notification of domestic and sexual violence was included in the National System of Notifiable Disorders and, in 2011, considered as a compulsory notifiable disorder. Establishment of this report sheet allowed a gradual increase in the number of notifications; at the start, there was a more sensitive glance over violence situations involving children and women and, later on, for those involving women and the elderly. Regarding the nature, physical violence is the most reported kind, followed by negligence, psychological violence and sexual violence. In an analysis of domestic accidents, especially among children, many situations of violence were identified, what lead us to see an interface between them.

Since then, GVE XXVII, complying to the guidelines proposed by the Ministry of Health and the State Secretary of Health, and in order to promote, within the area comprised by this regional branch, actions designed to prevent and offer attention to situations of violence, as well as promoting a culture of the peace, is promoting activities that raise awareness, update and support the cities as well as monitor information. Some strategies were developed to raise awareness and update managers, multidisciplinary teams with the objective to create an attention network able to recognize individual notifications and build a therapeutic project for families in a situation of violence; other initiatives include the creation of a Regional department for the deconstruction of violence, health promotion and culture of the peace (VIVA and Peace branch). This branch holds monthly meetings in which partners interchange information and support each other to promote surveillance actions in the cities.

With these objectives, updates were promoted, based on the conceptions of humanization, health surveillance and the pedagogic proposal of permanent education. Contents proposed allow: update of the staff to recognize signs of alert, support, notify, refer and act in a real network, as well as recognizing notification triggers protection and increases the visibility of violence. Facilitating knowledge of the epidemiologic profile, subsidizes public policies. The



desired result is the organization of municipal articulated departments with a conception focused on the acknowledgement of violence as a violation of rights and a public health problem implicating in the quality and the duration of life, besides promoting social inequalities.

Developing actions designed to increase attention and protection to the victims of violence, VIVA Peace, always aiming to establish network and coordinating partnerships has been promoting, since 2009, yearly regional seminars, always involving themes that interest the professionals of the network. These seminars have included relevant themes such as: culture of the peace, health promotion and social determinants, tourism and environmental changes as signs of alter for violence situations.

In 2013, the IV Seminar approached the theme “Protection Network: Essential connections for Human rights and Culture of the Peace Promotion”. The theme answered may signs presented by or partners, such as strengthening cross sector collaboration to encompass a complex theme. The objective was to broaden the reflection of Health Promotion and the development of a Culture of the Peace as possibilities for preventing situations of violence. The concepts of vulnerability and care were presented as mediators contributing to the diagnosis of the situation and the construction of singular and cross sector intervention projects in the protection network that may offer guidelines for public policies. Experiences in the development with innovations in the pedagogic approach in education and the change of paradigms in the justice were presented as examples to illustrate how these concepts can be translated into practices, as well as the project to build an inter sector network signaling the possibility to offer protection in situations of violence, such as the model developed by the health department/epidemiologic surveillance from Curitiba.

Seminars are clearly designed to bring light to questions that impact daily work and require theoretical and practical approached. They also facilitate the exchange of experiences among the professionals of the region, stimulating them to develop actions designed for persons in a situation of violence and increasing prevention through health promotion and creating a Culture of the Peace. Target public are all the professionals who direct or indirectly integrate the protection network (health, education, social welfare, Guardianship Councils, public safety, justice, culture and leisure, sports, NGOs and others). It is important to remind that these events were always discussed with the mentioned partners and count with the intense support of the National Service for Commercial Apprenticeship (Serviço Nacional de Aprendizagem Comercial – SENAC), through the social network.

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## AGENDA

27/3/2014 – 9 a 10/4/2014 e 7 e 8/5/2014



### International Debate Cycle on Public Policies for Nosocomial Infections and Patient Safety

The Nosocomial Infection Division is responsible for the coordination of the Prevention and Control Program for Infections Related to the Health Assistance (IRAS) in the State of São Paulo. The discussion on public policies designed for the prevention of nosocomial infections and patient safety, encompassing the scientific community, public policy makers and practitioners involved with the prevention and control of nosocomial infections and patient safety is one of the subjects under responsibility of the State Coordination.

The event is designed to increase the discussion on the search for the definition of applicable strategies, as well as to share experiences and identify lacks in the investigation, aiming to improve patient safety at institutional and governmental levels.

#### Target Public:

- University researchers of national and international institutions, involved in researches and studies along the thematic axes proposed;
- Professionals working at the State Coordination for Nosocomial Infection branches in Brazil;
- Professionals from the National Sanitary Surveillance Agency;
- Post graduate students.
- Profissionais do Ministério da Saúde;
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Data	Março	Local	Endereço
26-27 de Março	Resistência antimicrobiana nas instituições e na comunidade	Escola de Enfermagem, Universidade de São Paulo.	Av. Dr. Eneas de Carvalho Aguiar, 419. São Paulo
9-10 de Abril	Sistemas de vigilância e desenvolvimento de recursos humanos para prevenção de infecções relacionadas à assistência à saúde e segurança do paciente	Secretaria de Estado da Saúde de São Paulo.	Auditório José Ademar Av. Dr Arnaldo, 351, térreo. São Paulo.
7-8 de Maio	Impacto do cenário externo sobre os serviços de saúde: efeitos das epidemias e de grandes problemas endêmicos	Escola de Enfermagem, Universidade de São Paulo.	Av. Dr. Eneas de Carvalho Aguiar, 419. São Paulo

Inscrições: [www.cve.saude.sp.gov.br](http://www.cve.saude.sp.gov.br)

**27/3/2014**

**São Paulo strategies for cholera prevention in mass events**

Organized by: Disease Control Coordination and Epidemiologic Surveillance Center – Airborne and Foodborne Diseases Division

Local: Dr. Arnaldo, 351 – Anfiteatro Luiz Musolino – SES/SP

Registration: [www.cve.saude.sp.gov.br](http://www.cve.saude.sp.gov.br)

**April 24<sup>th</sup> to 26<sup>th</sup>, 2014**

**VII Hepatoaids**

Viral Hepatitis Division

Hotel Maksoud Plaza – São Paulo/SP

**May13<sup>th</sup>**

**VIII State Symposium on Influenza**

Taking into account the start of influenza season in the State of São Paulo, as well as the FIFA World Cup Brazil 2014TM, the “VII State Symposium on Influenza” will be held, next May. This event is designed to provide updated information in the epidemiology, clinical management and treatment of influenza.

This event is designed to update technical directors of the Regional Epidemiologic Branches, municipal epidemiologic surveillance staff, professionals from the NHE and CCIH, as well as physicians from state and municipal health services, from public or private nature.

**Local:** Centro de Convenções Rebouças (Rebouças Convention Center)  
Av. Dr. Enéas de Carvalho Aguiar, 23 – Cerqueira César – São Paulo/SP.

Registration: [www.cve.saude.sp.gov.br](http://www.cve.saude.sp.gov.br)

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