What's New in Immunization

Raymond A. Strikas, MD
National Immunization Program

Hosted by Paul Webber
paul@webbertraining.com
www.webbertraining.com

Disclosures

- The speaker has no financial interest or conflict with the manufacturer of any product named in this presentation
- The speaker will discuss the use of acellular pertussis vaccine in a manner not approved by the U.S. Food and Drug Administration
- The speaker will discuss vaccines not currently licensed by the FDA

Topics For This Presentation

- Disease incidence and vaccine coverage
- Influenza vaccine
- Meningococcal vaccines
- Acellular pertussis vaccine for adolescents
- Vaccines of the near future

20th Century Annual and Current Morbidity of Vaccine-Preventable Diseases

Disease	20th Century Annual Morbidity†	2004†	Percent Decrease
Diphtheria	175,885	0	99.9%
Measles	503,282	37	99.9%
Mumps	152,209	258	99.8%
Pertussis	147,271	25,827	82.5%
Polio (paralytic)	16,316	0	100%
Rubella	47,745	10	99.9%
Congenital Rubella Syndrome	823	0	100%
Tetanus	1,314	34	97.4%
H. influenzae, type b and unknown (<5 yrs)	20,000‡	196**	99.1%

† Sources: CDC. *MMWR* 1999; 48:242-264. *MMWR* 2005;54:772-80.
‡ Data are estimated. Values in YELLOW = at or near record lows in 2004.
** Includes serotype b (19) and unknown serotype (177)

Vaccine-Preventable Diseases Eliminated from the United States

Disease	Last Case*
• Smallpox	1949
• Polio	1979
• Measles	1993
• Rubella	2004

*Indigenous case. Importations may occur except smallpox, which has been eradicated from the planet

2004* National Immunization Survey

Vaccine	Coverage	Change
DTaP4	86%	+1%
MMR	94%	+1%
Hepatitis B3	93%	+1%
PCV3	73%	+5%
Varicella	88%	+3%
4:3:1:3:3	81%	+2%

*Calendar year 2004 compared to CY2003
Source:www.cdc.gov/nip/coverage/NIS/04/toc-04.htm

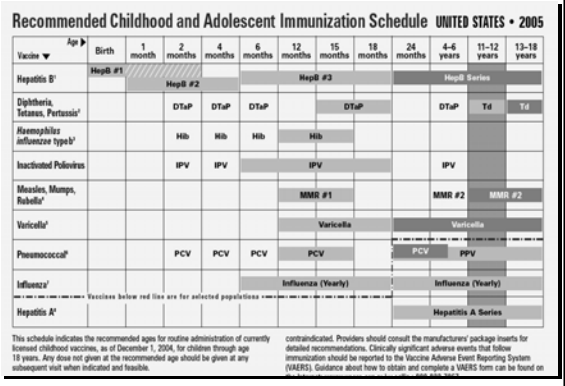
Why Immunization Coverage Levels Are So High

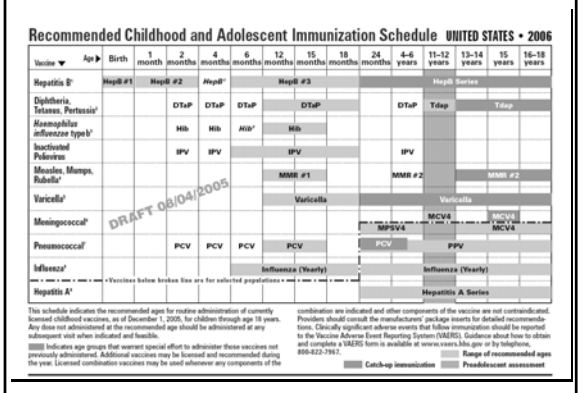
- Utilization of evidence-based strategies
  - Assessment of practice coverage levels with feedback to providers
  - Patient reminder / recall (including participation in immunization registry)
  - Provider prompting
  - Standing orders

Briss et al. *Am J Prev Med* 2000;18(1S):97–140)

2006 Childhood and Adolescent Immunization Schedule

- Similar format as 2005 schedule
- Td replaced with Tdap for 11-12 and 13-18 year olds
- Meningococcal conjugate vaccine added for 11-12 year olds
- Tdap and meningococcal vaccine footnotes added
- Minor wording changes in other footnotes
- Td catch-up schedule modified





Influenza Vaccine 2005-2006

- Sanofi Pasteur expected to produce 60 million doses
- Chiron expected to produce 18-26 million doses
- GlaxoSmithKline expected to produce about 8 million doses
- MedImmune expected to produce 3 million doses of LAIV

When Will I Get My Influenza Vaccine?

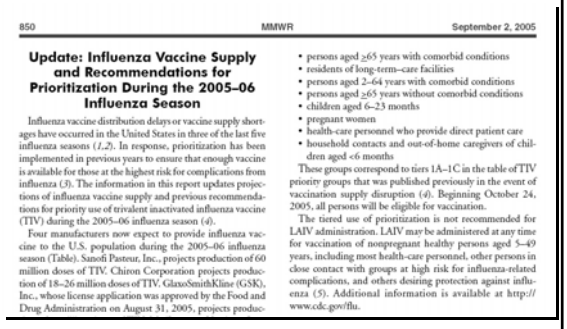
"As in previous years, the majority of sanofi pasteur customers will receive partial shipments through the end of September, with remaining shipments anticipated to arrive later in the season. This scheduling has proven beneficial over the past several years because it allows all customers to begin immunizing their priority patients early in the season. The company anticipates that the balance of customer requests will be shipped during October and November."

-statement by sanofi pasteur
29 Sepember 2005

Inactivated Influenza Vaccines Available* in 2005-2006

Vaccine	Package	Dose	Age	Thimerosal
Fluzone (sp)	Multi-dose vial	Age-dependent	≥6 mos	Yes
	Single dose syringe	0.25 mL	6-35 mos	No
	Single dose syringe	0.5 mL	≥36 mos	No
	Single dose vial	0.5 mL	≥36 mos	No
Fluvirin (Chiron)	Multi-dose vial	0.5 mL	≥4 yrs	Yes
	Single dose syringe	0.5 mL	≥4 yrs	Trace
Fluarix (GSK)	Single dose syringe	0.5 mL	≥18 yrs	Trace

*expected to be available as of September 27, 2005



850 MMWR September 2, 2005

Update: Influenza Vaccine Supply and Recommendations for Prioritization During the 2005–06 Influenza Season

Influenza vaccine distribution delays or vaccine supply shortages have occurred in the United States in three of the last five influenza seasons (*1*,*2*). In response, prioritization has been implemented in previous years to ensure that enough vaccine is available for those at the highest risk for complications from influenza (*3*). The information in this report updates projections of influenza vaccine supply and previous recommendations for priority use of trivalent inactivated influenza vaccine (TIV) during the 2005–06 influenza season (*4*).

Four manufacturers now expect to provide influenza vaccine to the U.S. population during the 2005–06 influenza season (Table). Sanofi Pasteur, Inc., projects production of 60 million doses of TIV. Chiron Corporation projects production of 18–26 million doses of TIV. GlaxoSmithKline (GSK), Inc., whose license application was approved by the Food and Drug Administration on August 31, 2005, projects produc-

- persons aged ≥65 years with comorbid conditions
- residents of long-term–care facilities
- persons aged 2–64 years with comorbid conditions
- persons aged ≥65 years without comorbid conditions
- children aged 6–23 months
- pregnant women
- health-care personnel who provide direct patient care
- household contacts and out-of-home caregivers of children aged <6 months

These groups correspond to tiers 1A–1C in the table of TIV priority groups that was published previously in the event of vaccination supply disruption (*4*). Beginning October 24, 2005, all persons will be eligible for vaccination.

The tiered use of prioritization is not recommended for LAIV administration. LAIV may be administered at any time for vaccination of nonpregnant healthy persons aged 5–49 years, including most health-care personnel, other persons in close contact with groups at high risk for influenza-related complications, and others desiring protection against influenza (*5*). Additional information is available at http://www.cdc.gov/flu.

Priority Groups for Influenza Vaccination

- Persons ≥65 years with comorbid conditions
- Residents of long-term-care facilities
- Persons 2-64 years with comorbid conditions
- Persons >65 years without comorbid
- Children aged 6-23 months
- Pregnant women
- Healthcare personnel who provide direct patient care
- Household contacts and out-of-home caregivers of children aged <6 months

*Vaccinate these groups now. After October 24 vaccinate everyone else (assuming supplies are adequate)
MMWR 2005;54(no. 34):850 (September 2, 2005)

Translation

- Comorbid: an underlying medical condition that increases the risk of complications of influenza (such as lung, heart, or kidney disease, diabetes, or immunosuppression)

Influenza Vaccine and VICP

- Influenza vaccine added to the Vaccine Injury Compensation Program as of July 1, 2005
- Includes both TIV and LAIV
- Persons of all ages are eligible
- Eight-year retroactive coverage
- See VICP website at www.hrsa.gov/osp/vicp for additional information

Live Attenuated Influenza Vaccine Indications

- Healthy* persons 5 – 49 years of age
  - –Close contacts of persons at high risk for complications of influenza (except contacts of severely immuno-suppressed persons)
  - –Persons who wish to reduce their own risk of influenza
- Not subject to "tiering"

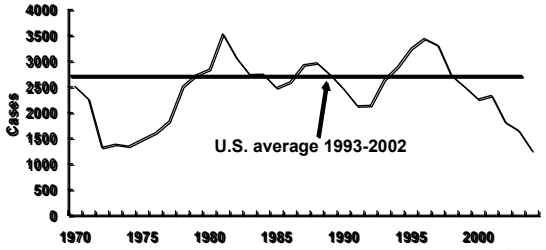
*Persons who do not have medical conditions that increase their risk for complications of influenza

Storage of LAIV

- Effective beginning influenza season 2005-2006 LAIV may be stored in a regular frost-free freezer*
- Manufacturer-supplied "freezebox" is no longer required
- May be stored up to 60 hours at refrigerator temperature but must be discarded if not used

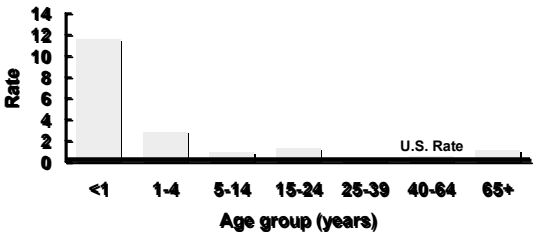
*Freezer with a separate door that reliably maintains an average of ≤-15°C

Meningococcal Disease – United States, 1972-2004*



*source: NETSS; 2004 provisional data

Meningococcal Disease, 1998 Incidence by Age Group



Rate per 100,000 population

Meningococcal Disease in the United States

- Highest rate is among children younger than 1 year of age
- About half of the cases occur in persons 15 years of age and older
- Strategy of infant immunization would require many years to impact burden of disease

Meningococcal Disease Among Young Adults, United States, 1998-1999

•18-23 years old	1.4 / 100,000
•18-23 years old not college student	1.4 / 100,000
•Freshmen	1.9 / 100,000
•Freshmen in dorm	5.1 / 100,000

Bruce et al, *JAMA* 2001;286;688-93

Meningococcal Disease in the United States

- Distribution of cases by serogroup varies by time and age group
- In 1996-2001:
  - –31% serogroup B
  - –42% serogroup C
  - –21% serogroup Y
  - –65% of cases among children <1 year of age due to serogroup B

CDC. ABCs unpublished data.

Meningococcal Polysaccharide Vaccine (MPV)

- Menomune® (sanofi pasteur)
- Quadrivalent (serogroups A, C, Y, W-135)
- Approved for persons ≥2 years of age
- Schedule: 1 dose, selective revaccination
- Administered by subcutaneous injection

Polysaccharide Vaccines

- Age-related immune response
- Not consistently immunogenic in children <2 years old
- No booster response
- Antibody with less functional activity

Meningococcal Conjugate Vaccine

- Menactra™ (sanofi pasteur)
- Quadrivalent (serogroups A, C, Y, W-135) conjugated to diphtheria toxoid
- Approved for persons 11-55 years of age
- Schedule: 1 dose, no revaccination
- Administered by intramuscular injection

Meningococcal Conjugate Vaccine

- Approved only for persons 11 through 55 years of age
- Persons 2-10 years of age >55 years at increased risk should receive the meningococcal POLYSACCHARIDE vaccine

Meningococcal Vaccine Recommendations

- Recommended for certain high-risk persons:
  - military recruits
  - certain research and laboratory personnel
  - travelers to and U.S. citizens residing in countries in which *N. meningitidis* is hyperendemic or epidemic
  - terminal complement component deficiency
  - HIV infection
  - functional or anatomic asplenia

MMWR 2005; 54(RR-7);1-21

Meningococcal Vaccine Recommendations

- Recommended for:
  - all persons at the preadolescent visit (ages 11-12 years)
  - persons about to enter high school (age 15 years)
  - college freshmen living in a dormitory
  - other adolescents who wish to reduce their risk for meningococcal disease

MMWR 2005; 54(RR-7);1-21

Meningococcal Vaccination for College Students

- ACIP recommends routine vaccination for college freshmen living in dormitories
- Colleges may choose to require vaccination for all matriculating freshmen
- Other students may elect to receive the vaccine

MMWR 2005; 54(RR-7);1-21

Meningococcal Vaccine Revaccination

- Revaccination may be indicated for persons at high risk for infection*
- Consider revaccination of children first vaccinated when they were <4 years of age after 2–3 years if they remain at high risk
- The need for revaccination of older children and adults has not been determined
- If indication still exists revaccination may be considered 5 years after first dose of MPSV

*e.g., persons who reside in areas in which disease is endemic (does not include college settings)

Meningococcal Vaccine Revaccination

- For persons 11-55 years of age, revaccination with MCV is preferred but MPV is acceptable
- MCV is expected to provide longer protection than the MPV
- Additional data regarding the need for MCV revaccination will become available within the next five years
- Continued attendance of college, or continued residence in a college dormitory is NOT an indication for revaccination in the absence of another indication (e.g., asplenia)

MMWR 2005; 54(RR-7);1-21

MCV Administration Errors

- Providers inadvertently administer MCV by the SC route
- There are NO DATA on the efficacy or safety of MCV given by the SC route
- sanofi pasteur recommends REPEATING the dose given SC
- CDC is collecting immunogenicity data to help guide revaccination recommendations

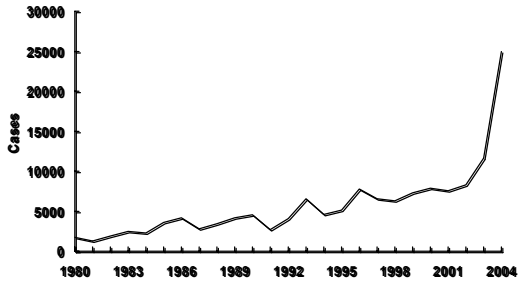
MCV "Shortage"

- Demand has been higher than anticipated
- Some providers have not all the vaccine they ordered
- CDC recommends providers limit vaccination to groups at increased risk until supply catches up with demand

Meningococcal Conjugate Vaccine (MCV) and GBS

- MCV approved by FDA in January 2005
- 2.5 million doses distributed
- 5 cases of GBS among 17-18 year olds within 4 weeks of MCV
- FDA/CDC advisory issued September 30, 2005
- No change in vaccine recommendations as of October 5, 2005

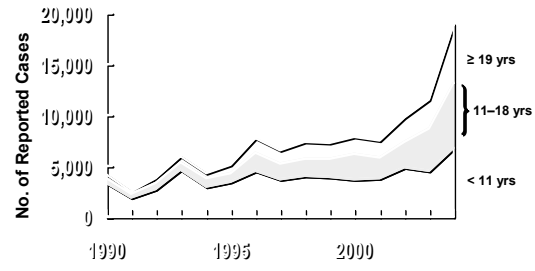
Pertussis – United States, 1980-2004



The Pertussis Paradox

- In 2004, pertussis vaccination levels among children 19-35 months of age were the highest ever recorded
- In 2004, the largest number of pertussis cases (25,827) was reported since 1959

Reported Pertussis by Age, United States - 1980-2004*



*2004 data provisional

Increase in Pertussis Among Older Children and Adults

- In 1997-2000, the pertussis incidence rate among adolescents and adults increased by 60%
- In 2003, 30% of reported pertussis cases were among persons 10-19 years of age
- >8,000 reported cases in this age group in 2004

Adolescent Pertussis Vaccination Objectives

- Primary
  - Protect vaccinated adolescents
- Secondary
  - Reduce *B. pertussis* reservoir
  - Potentially reduce incidence of pertussis in other age groups

Pertussis Among Adolescents

- Prolonged cough (more than 3 months)
- Loss of sleep
- Post-tussive vomiting
- Loss of consciousness
- Weight loss

Pertussis Among Adolescents

- Pneumonia (2%)
- Rib fractures (1%)
- Hospitalization (~1%)
- Medical costs
- Missed school and work
- Impact on public health system

Tdap Vaccines

- Boostrix™ (GlaxoSmithKline)
  - Licensed May 3, 2005
  - Approved for a single (booster) dose*
  - Approved for persons 10-18 years of age

*among persons who received a complete series of 4 or 5 dose of DTP/DTaP

Tdap Vaccines

- Adacel™ (sanofi pasteur)
  - Licensed June 10, 2005
  - Approved for a single (booster) dose*
  - Approved for persons 11-64 years of age

*among persons who received a complete series of 4 or 5 dose of DTP/DTaP

Composition of New Tdap Vaccines

	DTaP	Adacel	Boostrix
PT	10-25 µg	2.5 µg	8 µg
FHA	5-25 µg	5 µg	8 µg
PRN	3-8 µg	3 µg	2.5 µg
FIM	5 µg	5 µg	--
Dip	7-25 Lf	2 Lf	2.5 Lf
Tet	5-10 Lf	5 Lf	5 Lf

General Principles for Use of Tdap and Td Among Adolescents

- No preference for one brand over another*
- Tdap preferred to Td to provide protection against pertussis
- Licensed only for a single dose at this time
- Tdap not approved or recommended for children 7-9 years of age

*within the age limits approved by FDA for the individual vaccines

Provisional ACIP Recommendations for Tdap Vaccines

- Adolescents 11-12 years of age should receive a single dose of Tdap instead of Td*
- Adolescents 13-18 years who have not received Tdap should receive a single dose of Tdap as their catch-up booster instead of Td*

*if the person has completed the recommended childhood DTaP vaccination series, and has not yet received a Td booster

Provisional ACIP Recommendations for Tdap Vaccines

- ACIP encourages adolescents who received a Td booster to receive a single dose of Tdap to provide protection against pertussis*
- A 5-year interval between the Td and Tdap is encouraged to reduce the chance of a local reaction

*if the person has completed the recommended childhood DTaP vaccination series

Minimum Interval Between Td and Tdap

- Interval between Td and Tdap may be shorter if protection from pertussis needed
- ACIP did not define an absolute minimum interval between Td and Tdap
- Provider will need to decide based on whether the benefit of pertussis immunity outweighs the risk of a local adverse reaction

Deferral of Td

- Many providers have not yet received a supply of Tdap
- Providers may defer a scheduled dose of Td (in lieu of Tdap in the near future) if:
  - Last dose of tetanus-containing vaccine within the last 10 years, AND
  - Does not need immediate protection from tetanus, AND
  - Child likely to return for a subsequent visit when Tdap is available

Tdap For Persons Without A History of DTaP

- All adolescents should have documentation of having received a series of DTAP, DTP, DT, or Td
- Persons without documentation should receive a series of 3 vaccinations
- Preferred schedule:
  - Single dose of Tdap*
  - Td at least 4 weeks after the Tdap dose
  - Second dose of Td at least 6 months after the Td dose

*off-label recommendation

Tdap Contraindications and Precautions

- Contraindications and precautions for Tdap are different than those for either Td or DTaP
- (see handout)

Tdap Contraindications

- Severe allergic reaction to a vaccine component or following a prior dose
- Encephalopathy within 7 days of administration of a pertussis vaccine that is not attributable to another identifiable cause

Tdap Precautions

- History of an Arthus-type reaction following a previous dose of tetanus- or diphtheria-containing vaccine
- Progressive neurological disorder, uncontrolled epilepsy, or progressive encephalopathy
- Severe (anaphylactic) latex allergy
- History of Guillain-Barre' syndrome (GBS) within 6 weeks after a previous dose of tetanus toxoid-containing vaccine
- Moderate or severe acute illness

Conditions NOT Precautions for Tdap

- Following a dose of DTaP/DTP:
  - Temperature 105° F (40.5° C) or higher
  - Collapse or shock-like state
  - Persistent crying lasting 3 hours or longer
  - Convulsions with or without fever
  - History of an extensive limb swelling reaction

Conditions NOT Precautions for Tdap

- Stable neurological disorder
- Pregnancy
- Breastfeeding
- Immunosuppression including HIV infection
- Intercurrent minor illness
- Antibiotic use

TETANUS, DIPHTHERIA PERTUSSIS (Tdap) VACCINE

WHAT YOU NEED TO KNOW

1 Why get vaccinated?

Tdap (Tetanus, Diphtheria, Pertussis) vaccine can protect adolescents against three serious diseases.

Tetanus, diphtheria, and pertussis are all caused by bacteria. Diphtheria and pertussis are spread from person to person. Tetanus enters the body through cuts or wounds.

TETANUS (Lockjaw) causes painful tightening of the muscles, usually all over the body.
- It can lead to "locking" of the jaw so the victim cannot open his mouth or swallow. Tetanus leads to death in up to 2 cases out of 10.

DIPHTHERIA causes a thick covering in the back of the throat.
- It can lead to breathing problems, paralysis, heart failure, and even death.

PERTUSSIS (Whooping Cough) causes coughing spells that can make it hard to eat, drink, or breathe.
- It can lead to pneumonia, seizures (jerking and staring spells), brain damage, and death, especially in infants. In 2004 there were more than 25,000 cases of pertussis in the U.S. More than 8,000 of these cases were among adolescents 11-18 years of age. Up to 2 in 10 adolescents

3 Who should get Tdap vaccine and when?

Adolescents 11 through 18 years of age should get one booster dose of Tdap. Later booster doses should be given using Td.
- A dose of Tdap is recommended for adolescents who have gotten DTaP or DTP as children but not gotten a dose of Td. The preferred age is 11-12.
- Adolescents who have already gotten a booster dose of Td are encouraged to get a dose of Tdap as well, for protection against pertussis.

Adolescents who did not get all their scheduled doses of DTaP or DTP as children should complete the series using a combination of Td and Tdap.

An adolescent who gets a severe cut or burn might need protection against tetanus infection. Tdap may be used if the person has not had a previous dose. Otherwise, Td is recommended.

Tdap may be given at the same time as other vaccines.

4 Some people should not get Tdap vaccine or should wait.
- Anyone who has had a life-threatening allergic

Tdap for Persons 19 Years and Older

- Current ACIP recommendations include only persons 11-18 years of age
- ACIP Pertussis Working Group now addressing Tdap vaccination of persons 19 years and older
- Recommendations not likely until 2006
- Boostrix not approved for persons older than 18 years
- Providers may use Adacel for persons 11-64 years according to labeling (single dose only in person with complete DTP/DTaP series)

Vaccines on the Horizon

- New combinations
- Rotavirus (not Rotashield)
- Herpes zoster (shingles)
- Human Papillomavirus (cervical cancer and genital warts)
- Vaccines for sexually transmitted infections (HSV, GC)

MMRV (ProQuad)

- Combination measles, mumps, rubella and varicella vaccine
- Approved by FDA in September 2005 for children 12 months through 12 years of age (to age 13 years)
- Requires varicella vaccine storage conditions (i.e., <5°F at all times)
- May facilitate a recommendation for second dose of varicella vaccine

MMRV (ProQuad)

- MMRV is not just MMR and varicella vaccines mixed together
- Titer of varicella vaccine virus in MMRV is more than 15 time higher than standard Varivax
- Do NOT try to mix up your own MMRV
- Use only MMRV supplied by Merck

Herpes Zoster Vaccine

- Administered to persons who had chickenpox to reduce the risk of subsequent development of zoster
- Higher titer of varicella vaccine virus than standard Varivax®
- Results of clinical trial published in NEJM June 2, 2005
- Merck has filed BLA

Herpes Zoster Vaccine Trial

- 36,716 persons 60-80+ years of age followed for average of 3.12 years after vaccination
- Compared to the placebo group the vaccinated group had
  - 51.3% fewer episodes of HZ
  - Less severe illnesses
  - 66.5% less postherpetic neuralgia
- No significant safety issues identified

Oxman et al, *NEJM* 2005;352(22):2271-84

National Immunization Program
Contact Information

- Hotline (800) CDC-INFO
- Email nipinfo@cdc.gov
- Website www.cdc.gov/nip
- Vaccine Safety

www.cdc.gov/nip/vacsafe/concerns/gen/of-interest.htm

Infection Control Week Teleclasses

For more information, refer to www.webbertraining.com/schedule.cfm

October 17 – Glutaraldehyde Toxicology and Management of Risk
With Dr. Christie Forrester
Sponsored by Dow www.dow.com

October 18 – Tea Tree Oil and Resolving Bacterial Infections
With Dr. Linda Halcon

October 19 – New W.H.O. Hand Hygiene Guidelines
With Prof. Didier Pittet
Sponsored by Deb Canada www.debcanada.com

October 20 – Strategies for Adult Learners
Sponsored by Trainer's Resource for Infection Control
www.trainers-resource.com

Questions? Contact Paul Webber paul@webbertraining.com