Minnesota House of Representatives

Preventive Health Policy Division

Informational Overview of Childhood Vaccination

February 3, 2021

Proposed Agenda

John D. Grabenstein, RPh, PhD, ScD(Hon)

- Vaccine Development, Testing, & Monitoring
- Vaccines and Religion

Robert M. Jacobson, MD, FAAP, Mayo Clinic

- Vaccines, Vaccine Hesitancy, & Current Vaccine Practices

John D. Grabenstein, RPh, PhD, ScD(Hon)

Colonel (Retired), U.S. Army	1979 – 2006
Director, Military Vaccine Agency	
Merck Vaccines	2006 – 2020
Executive Director, Global Medical Affairs	
Vaccine Dynamics (consulting)	2020 – present
Sole proprietor	
Editor, Immunization Action Coalition (*immunize.org*)	

Easton, Maryland, USA

Nomenclature: Vaccine

vaccine n. (vak-SEEN) –
medication administered to trigger an immune response against a specific disease or infection

Vaccines do not protect directly.
Vaccination induces immunity against a future infection.

Vaccine Expectations

Other than clean water,
no other medical intervention has saved more lives.

Society's expectation: Vaccines must be the safest of all medications

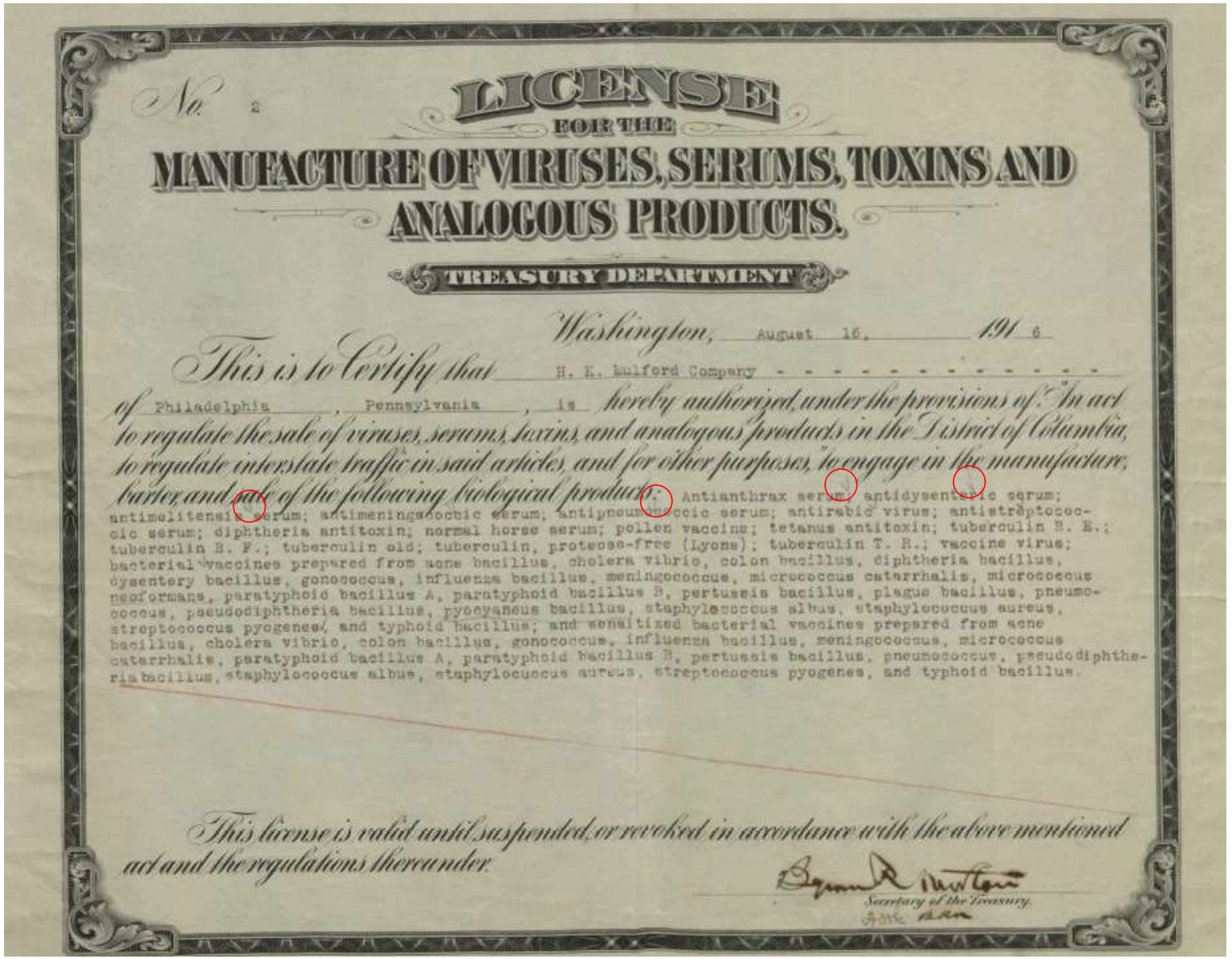
- To keep healthy people healthy.
- Before FDA licensing, vaccines are studied in larger populations than other drugs.
- Once licensed, multiple layers of safety surveillance continue as long as vaccines are distributed.

Vaccines Regulated by US Government since 1902

Licenses issued annually by US Dept. of Treasury after unannounced, on-site inspection

US License #2.
H.K. Mulford Co., 1916

Note check marks



No. 2

LICENSE
FOR THE
MANUFACTURE OF VIRUSES, SERUMS, TOXINS AND ANALOGOUS PRODUCTS.

TREASURY DEPARTMENT

Washington, August 16, 1916

This is to Certify that H. K. Mulford Company - - - - - - - - - - - - - - -

of Philadelphia, Pennsylvania, is hereby authorized under the provisions of "An act to regulate the sale of viruses, serums, toxins, and analogous products in the District of Columbia, to regulate interstate traffic in said articles, and for other purposes," to engage in the manufacture, barter, and sale of the following biological products: Antianthrax serum; antidysenteric serum; antimelitensis serum; antimeningococcic serum; antipneumococcic serum; antirabic virus; antistreptococcic serum; diphtheria antitoxin; normal horse serum; pollen vaccine; tetanus antitoxin; tuberculin B. E.; tuberculin B. F.; tuberculin old; tuberculin, protease-free (Lyons); tuberculin T. R.; vaccine virus; bacterial vaccines prepared from acne bacillus, cholera vibrio, colon bacillus, diphtheria bacillus, dysentery bacillus, gonococcus, influenza bacillus, meningococcus, micrococcus catarrhalis, micrococcus neoformans, paratyphoid bacillus A, paratyphoid bacillus B, pertussis bacillus, plague bacillus, pneumococcus, pseudodiphtheria bacillus, pyocyaneus bacillus, staphylococcus albus, staphylococcus aureus, streptococcus pyogenes, and typhoid bacillus; and sensitized bacterial vaccines prepared from acne bacillus, cholera vibrio, colon bacillus, gonococcus, influenza bacillus, meningococcus, micrococcus catarrhalis, paratyphoid bacillus A, paratyphoid bacillus B, pertussis bacillus, pneumococcus, pseudodiphtheria bacillus, staphylococcus albus, staphylococcus aureus, streptococcus pyogenes, and typhoid bacillus.

This license is valid until suspended or revoked in accordance with the above mentioned act and the regulations thereunder.

Secretary of the Treasury.

interstate traffic in said articles, and for other purposes, to engage in the

manufacture of the following biological products: Antianthrax serum; antidysenteric
erum; antimeningococcic serum; antipneumococcic serum; antirabic virus; antis
heria antitoxin; normal horse serum; pollen vaccine; tetanus antitoxin; tuber
; tuberculin old; tuberculin, proteose-free (Lyons); tuberculin T. R.; vaccin
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hylococcus albus, staphylococcus aureus, streptococcus pyogenes, and typhoid

FDA U.S. FOOD & DRUG ADMINISTRATION

Vaccine Development – 101

Development & Approval Process (CBER)

2020 Biological Approvals

2019 Biological Approvals

www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101

Manages overall program responsibilities, primarily lot release, review of application-based submissions, inspections.

- Reviews, evaluates, and acts on Investigational New Drug applications (INDs), marketing applications submitted to CBER.
- Performs Chemistry, Manufacturing, and Controls (CMC) and Current Good Manufacturing Practice (CGMP) reviews.
- Performs quality-assurance review of completed submissions for consistency in content as well as administrative proce

Product Release Branch

- Develops and administers biological products lot-release program.
- Receives, maintains, and distributes samples of biological products submitted for testing.
- Provides final quality review for lot release submissions and prepares release correspondence.

Manufacturing and Review Branches 1 and 2

- Meets with manufacturers to review facility design/CGMP/new products and technologies.
- Leads prelicense and preapproval inspections supporting Biologics License Application submissions and supplements.
- Prepares inspection reports as part of an inspection team and evaluates firms' corrective actions.

Applications Review Branch

- Prepares review packages and correspondence for final action. Schedules and coordinates meetings with industry.
- Issues and reissues U.S. and biologics licenses.

https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/division-manufacturing-and-product-quality-dmpq

Vaccine Components	Examples
Active ingredients	Weak or inactive viruses or bacteria: whole or subunit
Adjuvants (*adjuvare* – to help)	Aluminum, CpG1018
Preservatives (multidose vials only)	Phenol, phenoxyethanol, thimerosal
Stabilizers	Albumin, gelatin, histidine, pH buffers, lipids
Residuals from manufacturing process	Egg protein, cellular protein, formalin, surfactants

All ingredients from validated sources, all known and accepted by FDA

Phases of Vaccine Research & Development

Phase	Primary Goal	Dose Tested	# of Volunteers	Notes
Discovery	Plausible approach to prevention			
Preclinical Studies: Cell cultures (*in vitro*), Animal studies (*in vivo*)	Immune response, pharmacokinetics, toxicity			
Clinical Studies: Phase 1	*First-in-human:* Safety, immune response	Multiple: Dose-ranging	Dozens	FDA must permit
Phase 2	Safety, immune response	Expected dose (perhaps two)	Hundreds	FDA must permit
Phase 3 ("pivotal")	Safety, prevention of disease	Expected dose	*Drugs*: 100s to 1,000s *Vaccines*: Tens of 1,000s	FDA must permit
Approval of drugs. Licensure of vaccines.				FDA decision
Phase 4, post-marketing surveillance	Ongoing data collection for safety, durability, etc.		Hundreds of thousands, millions of recipients	FDA typically requires

Vaccine Safety Monitoring

CDC + FDA + Universities + DoD + IHS + etc

www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

Programs ranked by scientific power to explore cause-and-effect

Database Studies Comparing Millions of Recipients to Non-recipients:
Vaccine Safety Datalink,
DMSS, BEST,
Sentinel Initiative

Personalized Analysis of Cases by Expert Clinicians
CISA Project

Case Reports from Any Source
VAERS

Expanded Safety Monitoring Systems

The following systems and information sources add an additional layer of safety monitoring, giving CDC and FDA the ability to evaluate COVID-19 vaccine safety in real time and make sure COVID-19 vaccines are as safe as possible:

- **CDC:** V-safe — A new smartphone-based, after-vaccination health checker for people who receive COVID-19 vaccines. **V-safe** uses text messaging and web surveys from CDC to check in with vaccine recipients following COVID-19 vaccination. **V-safe** also provides second vaccine dose reminders if needed, and telephone follow up to anyone who reports medically significant (important) adverse events.
- **CDC:** National Healthcare Safety Network (NHSN) — An acute and long-term care facility monitoring system with reporting to the Vaccine Adverse Event Reporting System or VAERS that will allow for determination of COVID-19 vaccine adverse event reporting rates.
- **FDA: Other large insurer/payer databases** — A system of administrative and claims-based data for surveillance and research.

Existing Safety Monitoring Systems

As people get vaccinated, CDC, FDA, and other federal partners will use the following existing, robust systems and data sources to conduct ongoing safety monitoring:

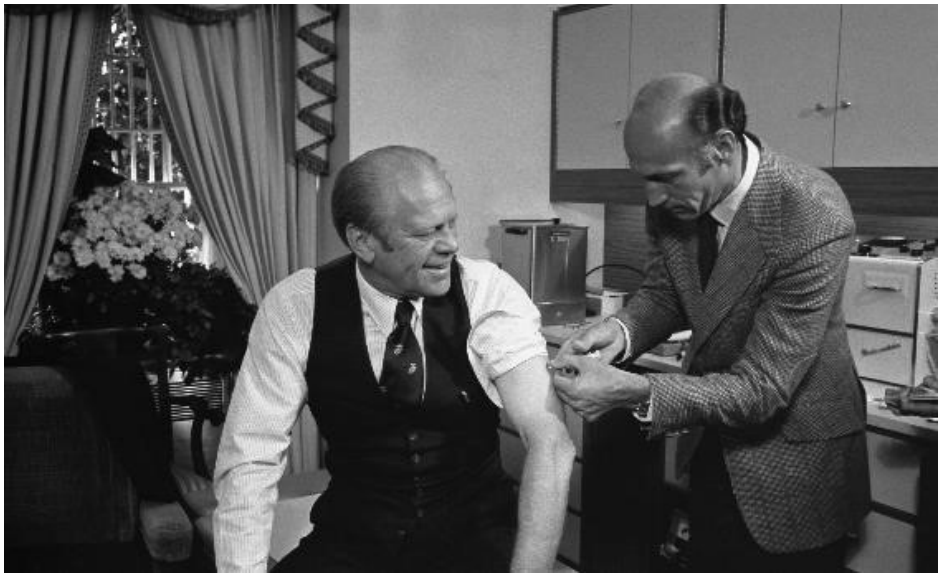
General public

- **CDC and FDA:** Vaccine Adverse Event Reporting System (VAERS) — The national system that collects reports from healthcare professionals, vaccine manufacturers, and the public of adverse events that happen after vaccination; reports of adverse events that are unexpected, appear to happen more often than expected, or have unusual patterns are followed up with specific studies
- **CDC:** Vaccine Safety Datalink (VSD) — A network of nine integrated healthcare organizations across the United States that conducts active surveillance and research; the system is also used to help determine whether possible side effects identified using VAERS are actually related to vaccination
- **CDC:** Clinical Immunization Safety Assessment (CISA) Project — A collaboration between CDC and 7 medical research centers to provide expert consultation on individual cases and conduct clinical research studies about vaccine safety
- **FDA and the Centers for Medicare and Medicaid Services: Medicare data** — A claims-based system for active surveillance and research
- **FDA:** Biologics Effectiveness and Safety System (BEST) — A system of electronic health record, administrative, and claims-based data for active surveillance and research
- **FDA:** Sentinel Initiative — A system of electronic health record, administrative, and claims-based data for active surveillance and research

Members of the military

- **Department of Defense (DOD):** DOD VAERS data — Adverse event reporting to VAERS for the DOD populations
- **DOD:** Vaccine Adverse Event Clinical System (VAECS) — A system for case tracking and evaluation of adverse events following immunization in DOD and DOD-affiliated populations
- **DOD: DOD Electronic Health Record and** Defense Medical Surveillance System — A system of electronic health record and administrative data for active surveillance and research

Swine Influenza Vaccination Program of 1976



Disease Alert

→ Mobilization of vaccine manufacturers

→ Mass vaccination program

Vaccine Safety

- October: Three people die of heart attacks on same day in Pittsburgh after vaccination.
  <u>Not related</u> to vaccine – Not higher than expected background rate.

- November: First reports of Guillain-Barré syndrome in vaccine recipients.
  <u>Caused by</u> vaccine -- ~ 4 times higher than expected rate in unvaccinated people.

Actual Influenza Cases

No further cases of swine flu to justify vaccination program.

Mobile Impfstation

Impf = vaccine in German

NY Times 2020 Dec 12

Standards for Vaccination

Inform and educate

- Train vaccine providers in vaccine administration, storage and handling, screening for contraindications, education of vaccinees, injection and related techniques, clinical ability to respond to adverse reactions

Vaccine storage and handling

- Maintain cold chain, refrigeration or freezing, as appropriate to the specific vaccine. Large stocks of vaccine inventories should be connected to recording thermometers and alarm systems

Assess immunization histories

- Identify earlier immunizations received and any adverse events to them

Assess contraindications

- Identify relevant contraindications that could make an immunization unsafe or unwarranted (e.g., relevant severe allergies, pregnancy, immune suppression)

Administer vaccine

- Administer the recommended dose by the proper route, observing safety and infection-control principles

Document

- Record the vaccinee's name, age, type of vaccine, dose, name of vaccine provider, date administered, manufacturer, and lot number

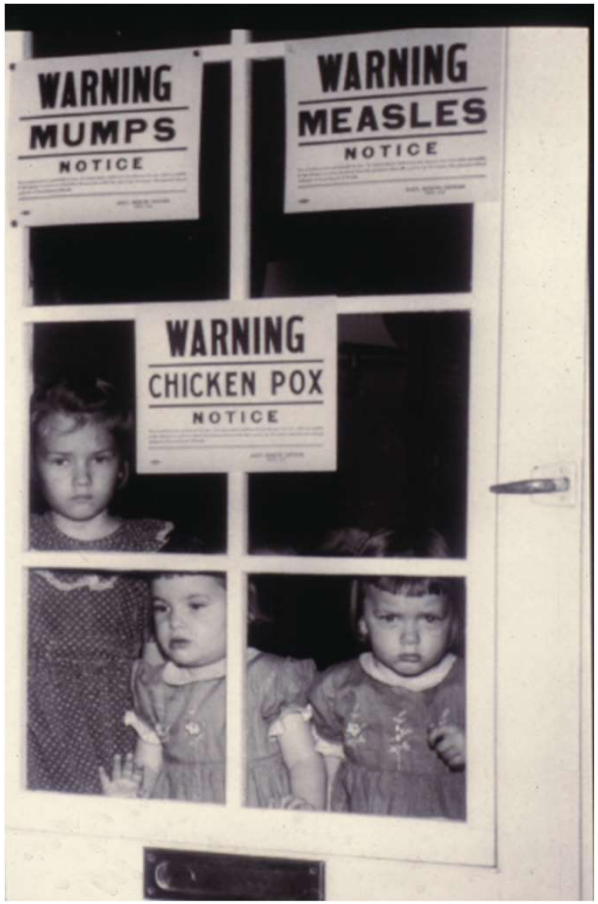
Monitor for adverse events

- Monitor patient for acute adverse reactions and treat appropriately. To improve knowledge about vaccine-associated adverse events, report adverse events to national authorities or program managers

Source:

Grabenstein JD, Nevin RL. Mass immunization programs: Principles and standards. *Curr Top Microbiol Immunol.* 2006;304:31-51.

American history is full of stories of terrible disease burdens, overcome by vaccination.



As vaccines intersect with people and society,

it is natural for there to be an intersection

of vaccines and religion.

What the world's religions teach, applied to vaccines and immune globulins

Grabenstein JD. *Vaccine.* 2013;31(Apr 12):2011-23.

Review of medical literature and Google top 50 hits.
Each religion with > 5 million adherents: Bahá'í Faith, Buddhism, Christianity, Confucianism, Daoism, Hinduism, Islam, Jainism, Judaism, Shinto, and Sikhism.

Also populous denominations within the Christian tradition: Amish, Anglican, Baptist, Church of Christ (Scientist), Church of Jesus Christ of Latter-day Saints ("Mormon"), Congregational, Dutch Reformed Congregations, Eastern Orthodox and Oriental Orthodox Churches, Episcopalian, Jehovah's Witnesses, Lutheran, Methodist, Pentecostal, Presbyterian, Roman Catholicism, and Seventh-Day Adventists.

Individual Rights ~ Collective Duties

- Individual rights
- Contagious diseases affect more than one person deciding for him/herself. Genesis 4:9: "…am I my brother's keeper?"
- Parental choices for children

- > 60 published reports of vaccine-preventable outbreaks among religious schools, congregations, communities
  - Diphtheria, *Haemophilus influenzae* b, hepatitis A, measles, mumps, pertussis, polio, rubella, tetanus
  - Across borders: from religious cohort to surrounding people
  - Measles and pertussis 6 to 35 times greater risk in people claiming religious exemption

What the world's religions teach, applied to vaccines and immune globulins

- **Jainism** Ahimsa: Respect for all living beings
  - Regretful acceptance of cooking, boiling water, paper, soap, antibiotics and vaccines.
- **Hinduism** Ahimsa: Respect for all living beings
  - No contemporary Hindu concerns with trace bovine components found.
- **Buddhism** Ahimsa. Treatment is an act of mercy.
  - Buddha's Sermon at Benares: "To keep the body in good health is a duty …
- **Judaism** *Pikuakh nefesh.* Duty to protect life. "Do not stand idly by"
  - Teach to swim. Fence on roof. Vaccinate on Sabbath. Kosher – oral only – not relevant to medication.
- **Christianity**
  - Mark 7:18-23: "Do you not see that whatever goes into a person from outside cannot defile … "
  - Christian Scientists: Disease not real, but rather an illusion by the devil.
- **Islam** Law to protect life, *izalat aldharar*, principle of public interest
  - Muhammad: "God has not made things that are unlawful for you to consume to be your medicine"

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The New York Times

Covid-19 Vaccines › | Vaccine Questions | Which States are Increasing Access | Rollout by State | How 9 Vaccines Work

Pope Calls Coronavirus Vaccinations an Ethical Obligation

Saying he will be vaccinated himself next week, Francis described the refusal to get the vaccine as suicidal.

www.nytimes.com/2021/01/09/world/europe/pope-coronavirus-vaccinations.html