Emergency Use Authorized COVID-19 Vaccines

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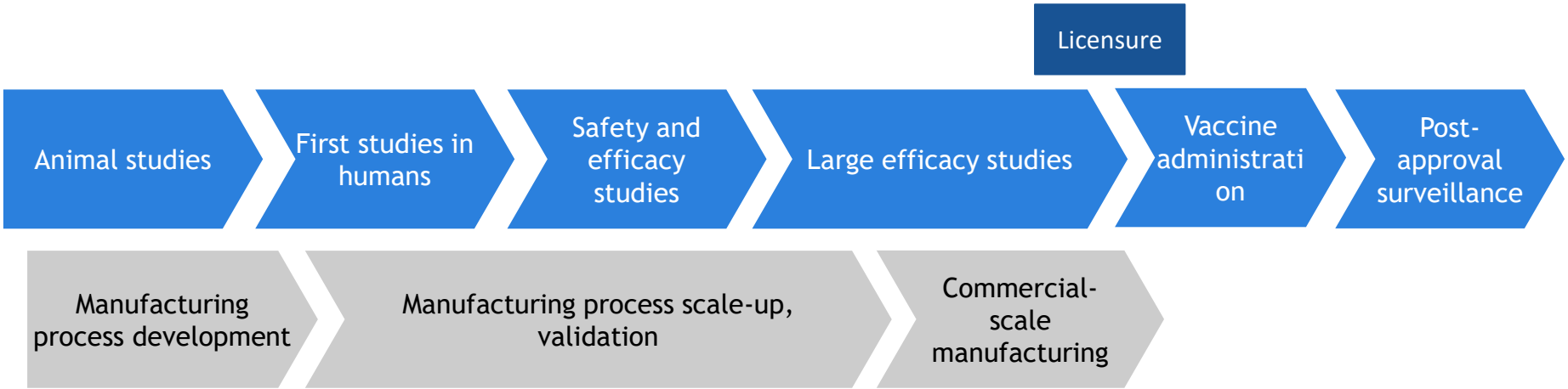
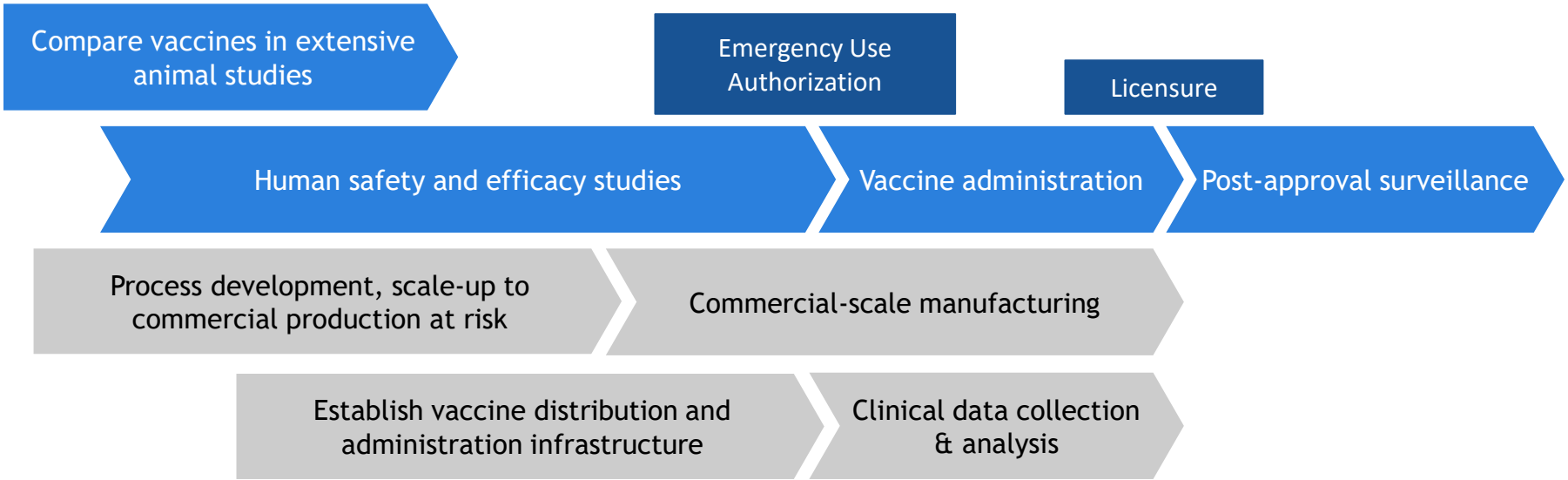
Traditional Vaccine Development



Accelerated Vaccine Development



Biologics License Application (BLA)

- Biologics are licensed under section 351 of the Public Health Service Act
- Product must be safe, pure, potent
- FDA considers evidence from adequate and well-controlled clinical trials

Emergency Use Authorization (EUA)

- Put in place after 9/11 to ensure that potentially lifesaving medical products could be available to people in medical need when there is not an approved and available alternative

- The standard used is that the product “may be effective” and its “known and potential benefits outweigh the known and potential risks”

EUA for a COVID-19 Vaccine

- FDA based authorization on clear and compelling efficacy in large well-designed phase 3 clinical trials
- Careful evaluation of quality, safety, efficacy
- Public advisory committee meeting
- Enhanced post-deployment surveillance

Advanced Candidates – June 2021

- mRNA
  - BNT162b2 (Pfizer-BioNTech) – EUA granted Dec 11, 2020
  - mRNA-1273 (Moderna) – EUA granted Dec 18, 2020

- Non-Replicating Viral Vector
  - Ad26.COV2.S (Janssen) – EUA granted Feb 27, 2021
  - ChAdOx1 (Astra Zeneca-Oxford)

- Protein Subunit
  - NVX-CoV2373 (Novavax)
  - MRT5500 (Sanofi-Translate Bio)

Vaccine Trial Demographics

Vaccine	Pfizer-BioNTech (2 doses 21 d apart)	Moderna (2 doses 28 d apart)	Janssen (1 dose)
Total patients	43,552	30,350	39,321
Receiving vaccine	21,768	15,180	19,630
Receiving placebo	21,784	15,170	19,691
Black/African Amer.	9.8%	9.7%	17.2%
Hispanic/Latino	26.2%	20.0%	45.1%
Am Indian/Alaska Native	0.6%	0.8%	8.3%
At least age 65	21.4%	25.3%	20.4%

Vaccine Efficacy in Phase 3

Primary efficacy was determined against moderate and severe/critical COVID-19

Vaccine	Pfizer-BioNTech	Moderna	Janssen
Primary efficacy (vaccinated/placebo)	95% (8/162)	94.1% (11/185)	d14 66.9% (116/348) d28 66.1% (66/193)
Young population	age 16-54 95.6% (5/114)	age 18-64 95.6% (7/156)	age 18-64 d14 63.7% (95/260) d28 66.1% (52/152)
Older population	age 55+ 93.7% (3/48)	age 65+ 86.4% (5/114)	age 65+ d14 76.3% (21/88) d28 66.2% (14/41)
Severe COVID-19	1/9	0*/30	d14 14/60; d28 5/34

*One severe case reported 2 months after vaccination

Vaccine Safety in Phase 3

		Second dose					
		Pfizer-BioNTech		Moderna		Janssen	
Reaction (2nd injection)	Placebo*	<55	55+	<65	65+	<60	60+
Injection site pain	14%	78%	66%	90%	83%	57%	33%
Fatigue	22%	59%	50%	68%	58%	44%	30%
Headache	21%	52%	39%	63%	46%	44%	30%
Muscle pain	10%	38%	29%	61%	47%	39%	24%
Chills	4%	35%	23%	48%	31%	N/A	N/A
Joint pain	8%	21%	19%	45%	35%	N/A	N/A
Fever	0.4%	16%	11%	17%	10%	13%	3%

*Average value across all studies, all doses, all ages

Pfizer Pediatric Demographics

Characteristic	Age 12-15 Vaccine (N=1131)	Age 16-25 Vaccine (N=537)	Age 12-15 Placebo (N=1129)	Age 16-25 Placebo (N=561)
Female	49.9%	52.5%	48.2%	52.0%
Mean Age (years)	13.6	19.4	13.6	19.6
Median Age	14.0	18.0	14.0	19.0
Black	4.6%	8.8%	5.0%	8.9%
Hispanic/Latino	11.7%	20.9%	11.5%	18.7%
Comorbidity (yes)	21.9%	23.5%	21.3%	25.7%

Pfizer Pediatric Immune Response

Study Group	12-15 Years N=190 GMT (95% CI)	16-25 Years N=170 GMT (95% CI)	GMT Ratio [12-15 Years/ 16-25 Years] (95% CI	Met Predefined Success Criterion
Vaccine	1239.5 (1095.5, 1402.5)	705.1 (621.4, 800.2)	1.76 (1.47, 2.10)	Yes

Noninferiority is declared if the lower bound of the 2-sided 95% CI for the Geometric Mean Titer (GMT) Ratio is greater than 0.67

Pfizer Pediatric Efficacy

Endpoint	Vaccine 12-15 Years N=1005 Cases	Placebo 12-15 Years N=978 Cases	Vaccine Efficacy % (95% CI)
First COVID-19 occurrence from 7 days after Dose 2 in subjects without prior SARS-CoV-2 infection	0	16	100.0 (75.3, 100.0)

Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period

Pfizer Pediatric Safety

Characteristic	Age 12-15 Placebo Dose 2 (N=1078)	Age 12-15 Vaccine Dose 2 (N=1097)	Age 16-25 Vaccine Dose 2 (N=488)
Injection site pain	17.9%	78.9%	77.5%
Fatigue	24.5%	66.2%	65.6%
Headache	24.4%	64.5%	60.9%
Muscle pain	8.3%	32.4%	40.8%
Chills	6.8%	41.5%	40.0%
Joint pain	4.7%	15.8%	21.9%
Fever	0.6%	19.6%	17.2%

Safety Monitoring by CDC and FDA

- Passive monitoring through the Vaccine Adverse Event Reporting System (VAERS) and the v-safe text monitoring system for COVID-19 vaccine safety

- Active monitoring through Vaccine Safety Datalink, the Clinical Immunization Safety Assessment, and large databases such as the CMS Medicare Database and Sentinel/BEST covering ≥100 million lives
  - Combination of claims data and EHR data
  - Monitoring about 15 safety outcomes of interest

Observed Safety Signals

- Severe allergic reactions (Pfizer-BioNTech, Moderna)
  - Rare anaphylactic reactions within about 30 minutes of vaccination
  - Mitigation strategy implemented (30-minute observation for those with history of allergic reactions)
- Thrombosis-thrombocytopenia syndrome (Janssen)
  - Rare cases of rare blood clots (mostly cerebral venous sinus thrombosis) and low blood platelets (thrombocytopenia) primarily in younger women
  - Information added to product label
- Myocarditis/pericarditis (Pfizer-BioNTech, Moderna)
  - Chest pain following vaccination associated with laboratory or imaging abnormalities primarily in younger individuals
  - Association still under investigation

COVID-19 Vaccine Development

- Vaccine development timelines shortened while still ensuring high vaccine safety and efficacy standards
- Vaccine authorization or approval has followed a process that has been as open to the public as possible
- A transparent process is important for facilitating vaccine confidence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