Background on Artificial Womb Technology

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FDA Presentations

- **Regulatory Considerations for Artificial Womb Technology (AWT) Development Programs**

  Kal Molla, MS

- FDA's Regulatory Safeguards for Children Involved in Clinical Trials: Considerations for AWTs

  Elizabeth L. Durmowicz, MD

- Clinical Considerations for Evaluating Benefit versus Risk for AWT Development Programs

  An Massaro, MD

- Animal Study Considerations for AWT Devices

  Annabelle Crusan DVM, MS

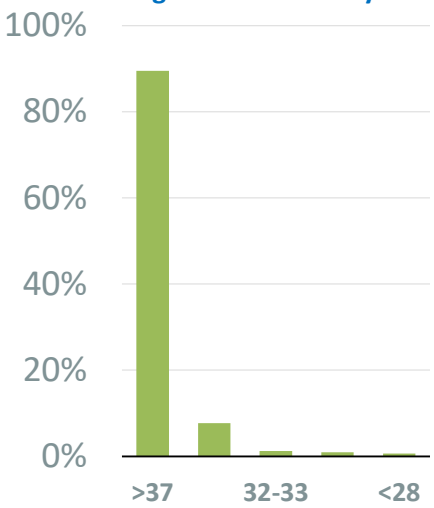
Outline

- Preterm birth background
- AWT device intended use and device descriptions
- Regulatory Considerations for AWT devices
  - AWT Device Classification
  - Early Feasibility Study

Preterm Birth in the US

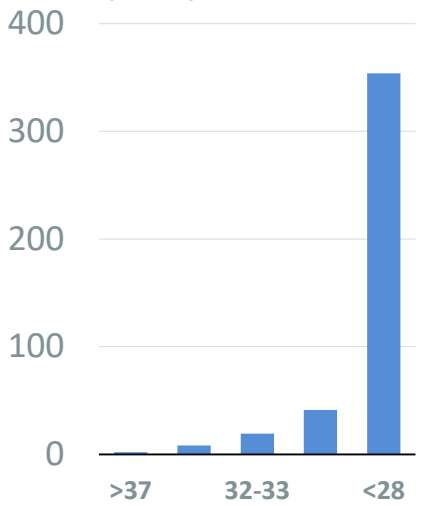
US Preterm Births

10%
of all livebirths are born preterm



US Infant Mortality

65%
of all infant deaths are born preterm



Preterm infants born <28 weeks gestational age

- **Represent 0.6% of all live births annually**
- **Account for 40% of all infant deaths**
- **High morbidity rates in survivors**

Source: NCHS 2021 period data [Data Access - Vital Statistics Online (cdc.gov)]

Intended Use of AWT

- Artificial womb technology (AWT) devices intend to treat extremely premature infants (EPIs) after 22 weeks GA
- AWT goal is to provide a bridge from extreme preterm birth to later gestation
- Potential AWT benefits
  - To reduce high mortality and long-term morbidity
  - To provide an environment to promote organ maturity
  - To provide stable gas exchange and hemodynamics
  - To reduce morbidity associated with mechanical ventilation

AWT Components

- System for sterile fluid submersion
- Oxygenator
- Umbilical cannulas
- Monitoring and display systems

Extracorporeal circuit configurations

Graphical representation of extracorporeal circuit configurations of published AP/AWT models

A) AP: VV (venovenous) UV/JV cannulation with pump and oxygenator

B) AWT: VA (venoarterial) UA/UV cannulation with dual oxygenator

C) AWT: VA (venoarterial) UA/UV cannulation with single oxygenator

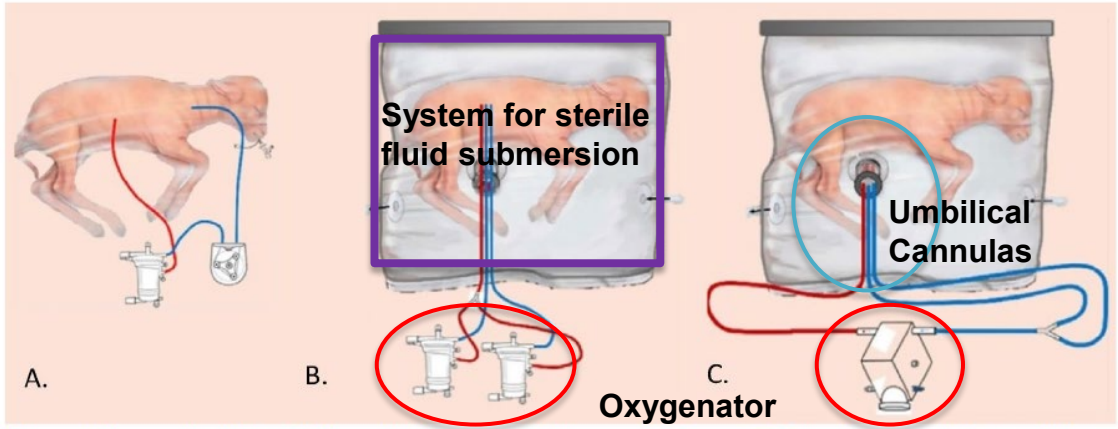


Figure 6. Source: De Bie et al, Prenatal Diag 2021 (Reference #31); reprinted in Spencer et al; Sem Fet Neonat Med 2022 (Reference #32)

AWT Regulatory Considerations

AWTs are Class III significant risk devices

- Class III devices are those that present the potential for serious risk to the health, safety, or welfare of a subject and may be:
  - an implant;
  - a life supporting or life sustaining device; or
  - a device of substantial importance in diagnosing curing, mitigating, or treating disease, or in otherwise preventing impairment of human health

Investigational Device Exemptions (IDEs)

- An IDE approval is issued by FDA to allow the use of *investigational* devices in humans in the US
  - IDE and IRB approval required ***before*** initiating enrollment
- An approved IDE provides protection to subjects via informed consent and study monitoring
- Clinical study data collected under an IDE can be used to support a device marketing application

CDRH's Early Feasibility Studies (EFS) Program

Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

Guidance for Industry and Food and Drug Administration Staff

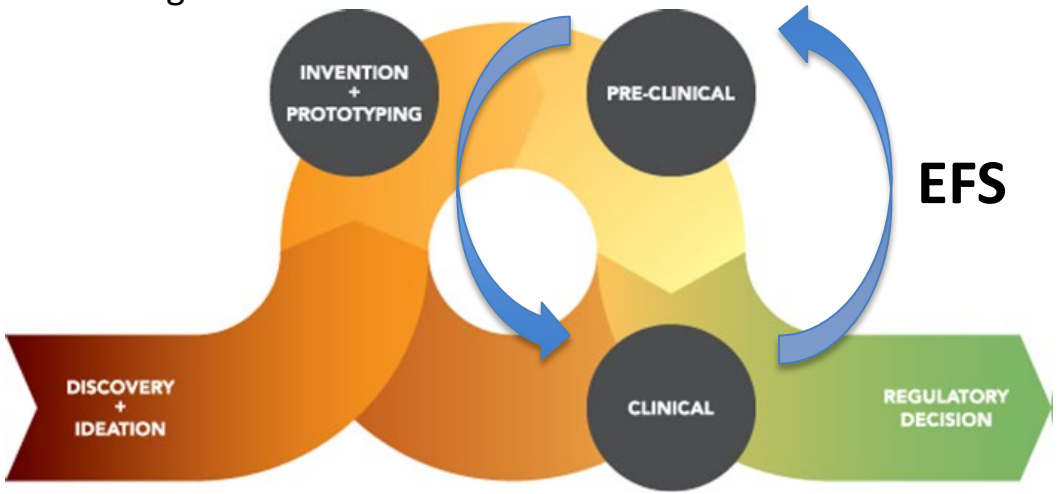
Document issued on: October 1, 2013

The draft of this document was issued on November 10, 2011.

For questions regarding this document, contact CDRH's Andrew Farb, 301-796-6343, Andrew.Farb@fda.hhs.gov or Dorothy Abel, 301-796-6366, Dorothy.Abel@fda.hhs.gov, or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

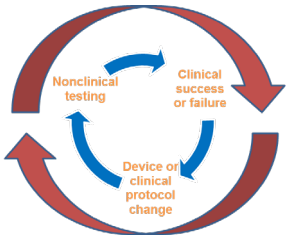
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

- Increase early **patient access** to potentially beneficial medical devices in the US
- Expand US site participation in the early clinical evaluation of innovative medical devices
- Enhance collaboration among developers, industry, regulators, and investigators
- Utilize the IDE regulations to protect study participants during the EFS



Early Feasibility Studies

- EFS definition
  - Small number of initial subjects
  - Device may be early in development, before device design has been finalized
  - Needed when information to advance device development cannot be practically obtained with additional nonclinical assessments, or nonclinical tests are unavailable
- EFS regulatory review considerations
  - Target clinical condition: Availability, effectiveness, and safety risks associated with alternative treatments (for extremely premature infants)
  - Investigational plan incorporates risk mitigation strategies, augmented monitoring, and tailored consent process to enhance patient safety



EFS IDE approval does not lower the fundamental regulatory requirements for initiating clinical studies of investigational SR devices

EFS Risk Mitigation Strategies Examples

- Choice of study sites and investigators with sufficient expertise and resources to manage adverse events and provide appropriate therapies
- Follow-up assessments at frequent intervals
- Timely reporting of serious adverse events to FDA
- A pre-specified plan for periodic patient outcome assessments and reporting

AWT EFS Proposal

- FDA will consider EFS principles in the evaluation of the AWT devices for IDE approval considering:
  - The high mortality and morbidity rates associated with EPIs
  - The challenges in developing nonclinical animal models
  - Novelty of AWT devices
- EFS IDE approval must still comply with fundamental regulatory requirements

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