

REGULATORY HURDLES FOR IVD COMPANIES

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WORLDWIDE FILING REQUIREMENTS

- 20 YEARS AGO – A HANDFUL OF COUNTRIES
- 10 YEARS AGO – APPROXIMATELY 54 COUNTRIES
- TODAY - APPROXIMATELY 112 COUNTRIES





Product Stewardship -
All stages of product life management, from
development through the end of the product life cycle

REQUIREMENTS NOW THROUGHOUT DEVELOPMENT PROCESS

Requirements are now placed all on PRE, ON Market, and POST Market periods



EUROPEAN UNION IN-VITRO DEVICE REGULATION (IVDR)

- **IVD REGULATION 2017/746/EU**

CHINA

CFDA

- NEW REQUIREMENTS INTRODUCED IN OCTOBER 2014
- DEFINITION OF IVDS
- SPECIFIC STANDARDIZATION PROPOSED
- SAMPLE TESTING AT A CFDA CERTIFIED TESTING CENTER IN CHINA
- ALMOST ALL CLASS II AND III IVD PRODUCTS REQUIRE LOCAL CLINICAL STUDIES.



SOUTH KOREAN MINISTRY FOR FOOD AND DRUG SAFETY (MFDS)

In-vitro Diagnostic Medical Devices Act

- New regulations for registration and labeling requirements of IVD products in order to improve oversight of these devices' safety and quality
- Will define IVD products
- Will include procedures for conducting clinical performance testing
- Effective May 2020
- Specific for IVDs; distinct from Medical Device Act of 2017



SAUDI FOOD AND DRUG AUTHORITY (SFDA)

- October 2019, fee increase for Medical Device Marketing Authorization (MDMA)
- Implementation of a new regulatory system in early 2020, with a new risk classification
Currently, an SFDA device registration is based on an existing approval in Australia, Canada, EU, Japan, or the USA



BRAZIL NATIONAL HEALTH SURVEILLANCE AGENCY (ANVISA)

- RDC 270/2019
- Implementation May 2019
- Established a new notification pathway for Class I medical devices and IVDs
- Removes requirements for full dossier submission and technical review
- Modifications to notified devices will be also be allowed



HARMONIZATION EFFORTS

- **GLOBAL HARMONIZATION TASK FORCE**

- THE GLOBAL HARMONIZATION TASK FORCE (GHTF) WAS FOUNDED IN 1993 BY THE GOVERNMENTS AND INDUSTRY REPRESENTATIVES OF AUSTRALIA, CANADA, JAPAN, THE EUROPEAN UNION, AND THE UNITED STATES OF AMERICA.
- ENCOURAGE A CONVERGENCE IN STANDARDS AND REGULATORY PRACTICES RELATED TO THE SAFETY, PERFORMANCE AND QUALITY OF MEDICAL DEVICES.

- **INTERNATIONAL MEDICAL DEVICE REGULATORS FORUM**

- THE INTERNATIONAL MEDICAL DEVICE REGULATORS FORUM (IMDRF) WAS CONCEIVED IN FEBRUARY 2011 AS A FORUM TO DISCUSS FUTURE DIRECTIONS IN MEDICAL DEVICE REGULATORY HARMONIZATION. REPRESENTATIVES OF AUSTRALIA, BRAZIL, CANADA, CHINA, JAPAN, THE EUROPEAN UNION, RUSSIA, SINGAPORE, SOUTH KOREA., AND THE UNITED STATES OF AMERICA.
- IT IS A VOLUNTARY GROUP OF MEDICAL DEVICE REGULATORS FROM AROUND THE WORLD WHO HAVE COME TOGETHER TO BUILD ON THE STRONG FOUNDATIONAL WORK OF THE GHTF, AND TO ACCELERATE INTERNATIONAL MEDICAL DEVICE REGULATORY HARMONIZATION AND CONVERGENCE.

INTERNATIONAL REQUIREMENTS

SIMILARITIES:

- LOCAL REPRESENTATIVE
- CERTIFICATE OF FREE SALE (COFS) OR CERTIFICATE TO FOREIGN GOVERNMENT (CFG)
- IMPORT LICENSE FROM THE COMPETENT AUTHORITY IN THE IMPORT COUNTRY
- REGISTRATION OF THE COMPANY AND THE PRODUCT

DIFFERENCES:

- IVD CLASSIFICATION
- TECHNICAL DOCUMENTATION TO SUPPORT REGISTRATION
- LEGAL DOCUMENTATION TO SUPPORT REGISTRATION
- REGISTRATION COSTS
- REGULATORY AUTHORITY APPROVAL TIMES
- MANAGEMENT OF PRODUCT CHANGES, RENEWALS, CERTIFICATIONS

CHALLENGES FOR IVD MANUFACTURERS COMPLIANCE

- NUMBER OF REGULATIONS
- REQUIRED DOCUMENTATION – NUMEROUS REPORTS CONTAINING THE SAME INFORMATION WITH DIFFERENT FORMATS – SOME COUNTRIES REQUIRE THESE DOCUMENTS BE UPDATED THROUGHOUT LIFE CYCLE
 - IVDR WILL LIKELY FORCE ONE FORMAT FOR BOTH EU AND US SUBMISSIONS
 - IVDR WILL LIKELY RESULT IN ALIGNING PRODUCT RELEASE IN EU AND US

HARMONIZATION WILL HELP REDUCE DOCUMENTATION BURDEN

CHALLENGES FOR IVD MANUFACTURERS PRE-MARKET REQUIREMENTS

- MULTIPLE CLASSIFICATION SYSTEMS FOR PRODUCTS
 - WHY ARE SAME ANALYTES CONSIDER DIFFERENT RISKS IN DIFFERENT POPULATIONS?
- MULTIPLE SOURCES OF STANDARDS – COUNTRY SPECIFIC
 - HOW CAN MANUFACTURERS BE EXPECTED TO STANDARDIZE TO MULTIPLE STANDARDS?
- DIFFERENT ANALYTICAL REQUIREMENTS
 - WHY ARE DIFFERENT ANALYTICAL REQUIREMENTS CONSIDERED FOR DIFFERENT POPULATIONS?
- DIFFERENT CLINICAL TRIAL REQUIREMENTS – LOCAL POPULATIONS
 - WHY ARE DIFFERENT CLINICAL STUDY REQUIREMENTS CONSIDERED FOR DIFFERENT POPULATIONS?
- BATCH RELEASE TESTING – EX. IVDR CLASS IN ANNEX II HIGH RISK LIST THE NOTIFIED BODY MUST VERIFY THE PRODUCT MEETS THE COMMON TECHNICAL SPECIFICATION (CTS) AND MUST RELEASE EACH BATCH OF PRODUCT BEFORE IT CAN BE PLACED ON THE EUROPEAN MARKET. THE BATCH RELEASE OFTEN REQUIRES TESTING.
 - IMPACT ON PRODUCT AVAILABILITY?

HARMONIZATION WILL HELP REDUCE DOCUMENTATION BURDEN BUT CLINICALLY MEANINGFUL OUTCOMES MUST PREVAIL OVER CHECKLISTS

MANUFACTURERS SHOULD JUSTIFY CLINICAL OR TECHNICAL RATIONALE AND GOVERNMENTS SHOULD CHALLENGE – FDA-PRESUB PROCESS IS VERY VALUABLE IN HELPING ENSURE TECHNICAL EVALUATIONS SUPPORT INTENDED USE CLAIMS. NOT CLEAR IF A SIMILAR PROCESS WILL BE AVAILABLE FOR IVDR.

CHALLENGES FOR IVD MANUFACTURERS POST MARKET REQUIREMENTS

- REPORTING POST-MARKETING ISSUES TO MULTIPLE COUNTRIES – CENTRALIZING WOULD IMPROVE REPORTING
- HARMONIZING RISK ASSESSMENTS FOR RECALLS
 - DIFFERENT PRACTICES ACROSS INDUSTRY
 - DIFFERENT EXPECTATIONS FROM DIFFERENT COUNTRIES
- MONITORING EMERGING RISKS
 - EX. BIOTIN (NONREGULATED TREATMENT) , THERAPEUTIC MAB (NONREGULATED TREATMENT), BSA (RAW MATERIAL CHANGES)
 - BETTER TO SPEND EFFORT MONITORING OR IN IMPROVING RAPID RESPONSE MEASURES?

WILL WE MEASURE IF REGULATIONS PROVIDE VALUE?

- DO IVDS POSE THE SAME RISK TO PATIENTS AS OTHER MED DEVICES?

/E. IMPLANTABLE VS. IVDS

US AND EU HAVE HAD VERY DIFFERENT SYSTEMS PRIOR TO IVDR. WAS THE EU POPULATION AT GREATER RISK FOR ISSUES WITH IVDS?

- IN US INTRODUCTION OF DESIGN CONTROL MEASURES HAVE IMPROVED QUALITY OF IVDS AND RESULTED IN BETTER BUSINESS GAINS
 - HAVE SEEN A DECREASE IN PRODUCTS GETTING TO MARKET WITH DESIGN FLAWS OR UNSUBSTANTIATED INTENDED USE IN PAST 20 YEARS
- ARE WE REACHING POINT OF DIMINISHING RETURNS? HOW WILL WE KNOW?

FOR COUNTRIES CONSIDERING NEW REGULATIONS — CAN HARMONIZATION GROUPS PROVIDE GUIDANCE IN ADVANCE OF ACTION?



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