

Regulatory Market Update: What are the major changes and differences worldwide?

Marlene E. Haffner MD, MPH, CEO
Haffner Associates
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Haffner
Associates, LLC

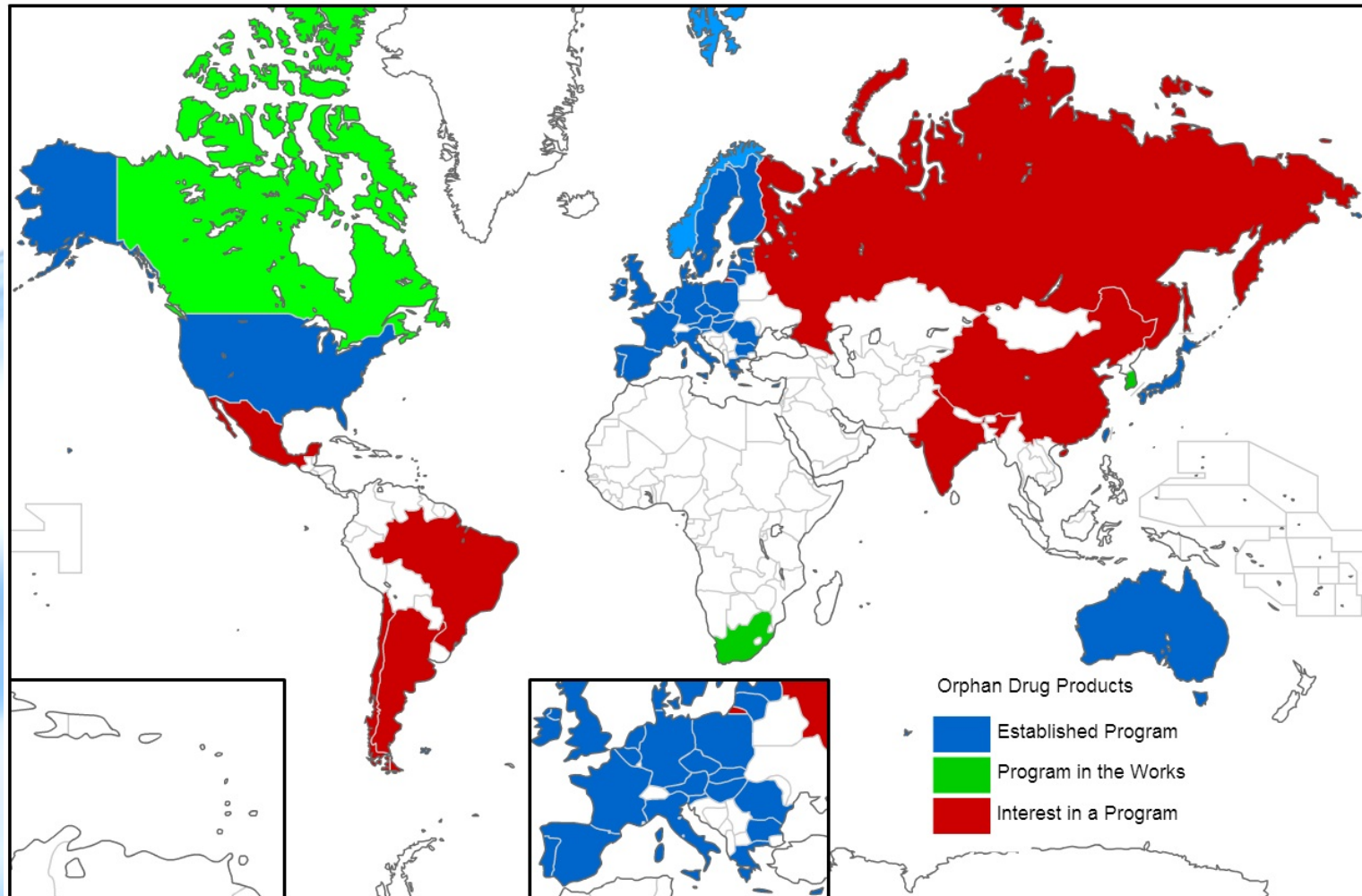
Expertise Orphan Products & Rare Diseases

Orphan Drug Landscape†

- Orphan Drugs are “IN”
- Estimated worth of the global market - \$50 Billion
- Percentage of orphan drugs with annual sales > 1 billion \$ - 29%
- Percentage of orphan drugs with additional rare disease indications – 15%
- 460+ Orphan products under FDA review in U.S. (2014)
- A record 291 orphan drug designations were granted in the US in 2014
 - 49 Orphan Products approved 2014
 - Same standards for review and approval as non-orphans “except” for FDA flexibility

† - Sources: NORD, Orphanet, Evaluate Pharma, PhRMA, Thomson Reuters, FDA

Where In The World Is Orphan Drug Policy



Orphan Drugs in US

- Orphan Drug Act (1983)
- Rare disease = prevalence < 200,000
- 7 Year Market Exclusivity
- FDA Filing Fee Wavier
- Tax Credits for clinical trials
- Orphan Product Grants
- ~494 drugs approved; >3400 designated (FDA)
- Use of accelerated approval/fast track/pediatric voucher/breakthrough designation



Common EMEA/FDA Application for Orphan Medicinal Product Designation

- Sponsor may apply for orphan designation of the same medicinal product for the same use in both jurisdictions by using this common application
- Still independent review from each agency
- FDA no longer requires a statement of party of interest for an orphan drug designation



Regulatory Changes

FDA

- investigational new drug application is filed with the FDA for drugs that appear safe in the preclinical phase
- Drug vs. placebo
- Phase 0 including therapeutic or diagnostic intent
- Biologics Price Competition and Innovation Act of 2009 (BPCI Act)

EMA

- Assessment is conducted by national agencies of member states
 - Enforcement is done by member states with help of EMA
- application for a marketing authorization license is filed with the EMA
- Drug vs existing drug
- Improving coordination
- Microdose trials

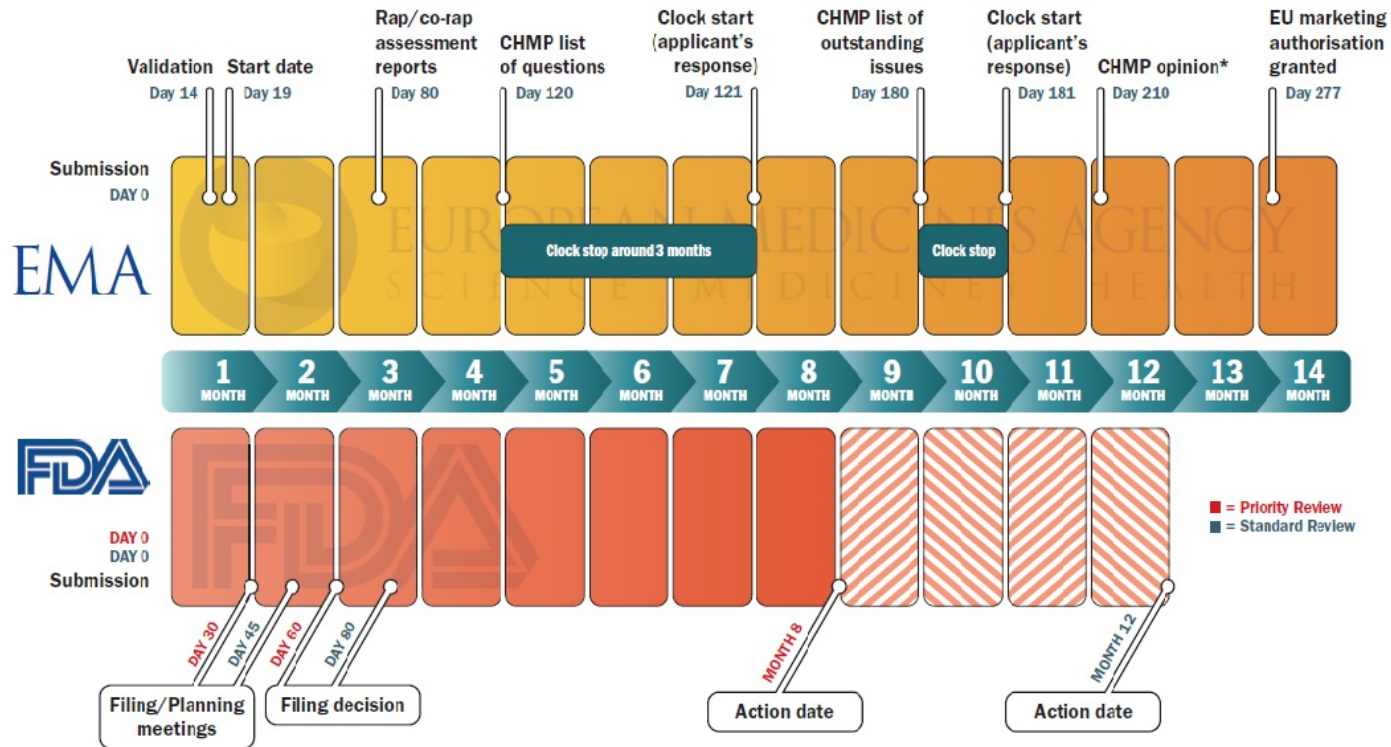


Regulatory Changes in Drug Approval Process

- Accelerated
 - **Serious conditions** that filled an unmet medical are permitted to be approved based on a surrogate endpoint
- Priority Review
 - 6 month response from FDA
 - 21st Century Act - emphasis on medical devices
- Fast Track
 - Facilitates development and expedites review for drugs that treat serious conditions and fill unmet medical need
- Breakthrough
 - Expedite development and review of drugs that demonstrate substantial improvement over available therapy
- Pediatric Voucher
 - Extends priority review for new drugs that are developed to treat rare pediatric diseases
 - Can be used in combination with other incentive programs
- Increased emphasis on safety – post approval monitoring



Approval Timeline



On average the EMA takes around six months more than the FDA to approve a new drug or new indication for a drug. This is mainly due to time lost to clock stop and the delay between getting a positive CHMP opinion and approval from the European Commission. Furthermore, in the US almost all cancer drugs are approved under priority review, whereas accelerated assessment is rarely used by the EMA

Source: CDER 21st Century Review Process (www.fda.gov); User Guide for Micro, Small and Medium-sized Enterprises (www.ema.europa.eu)

*Day 150 for accelerated assessment; Rap – Rapporteur



Challenges in developing drugs across borders

- Cultural differences
- Prescribing practices
- Trade agreements / parallel trade offers - IP
- Price Controls – who is paying?
- Direct-to-consumer (DTC) advertising
- Differences in regulation



21st Century Cures Act - US

- Increases funding for NIH and FDA
- Data Access
 - expand surveillance of neurological diseases
 - revise health information privacy rules
 - implement a system that allows further research on clinical trial data
- Orphan Product Extensions Now; Incentives for Certain Products for Limited Populations
 - Section 2151 - FFDCA is amended to extend market exclusivity by six months
 - Section 2152 - priority review voucher program
 - Extended for pediatric diseases through 2018
 - apply only to serious diseases
- Streamlining Clinical Trials
 - No consent required for medical devices that pose minimal risk
 - IRB reviews for clinical testing of medical devices no longer needs to be local



Open Act HR971- US

- Proposed legislation from the senate
- Extends market exclusivity by 6 months for repurposed drugs that are approved to prevent, treat, or diagnose a new indication of rare disease
 - Requires indication from FDA on label
- Requires FDA to inform the public of products that receive extension
- Limits the product for one extension
- Applies only to new indications after the Act is passed
- Extension can be revoked only through untrue statements on application



¿Questions?

Marlene E. Haffner, MD, MPH
President & CEO

11616 Danville Drive
Rockville, Maryland 20852

mhaffner3@verizon.net

301 984 5729 - office

301 641 4268 - cell

301 984 2272 - FAX



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