

EU Commercial Product Launches by OEU Companies

***David Downey – VP Commercial Operations
Almac Pharma Services***

12th May 2009



Agenda



- EU Market Opportunity
- EU Regulatory Background
- Role of QP for Imported Products
- Implications for Consideration
- Challenges
- Best Practice Guidelines
- Case study

EU Market Opportunity



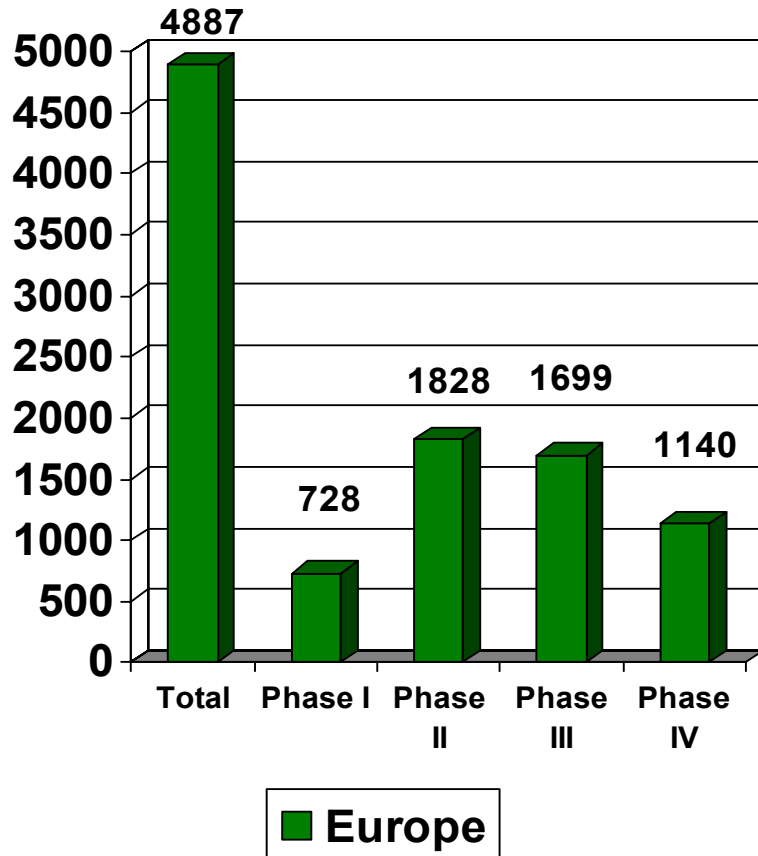
- 27 Member States and growing
- ~ 500 million citizens (in January 2009)
- Produces 30% share of gross world product and accounts for 31% of global pharmaceutical sales
- EU is < half the size of the US, but its population is > 50% larger
- 23 Official working languages
- 150 regional & minority languages



EU Market Opportunity



US Phase I, II & III Clinical Trials in Europe



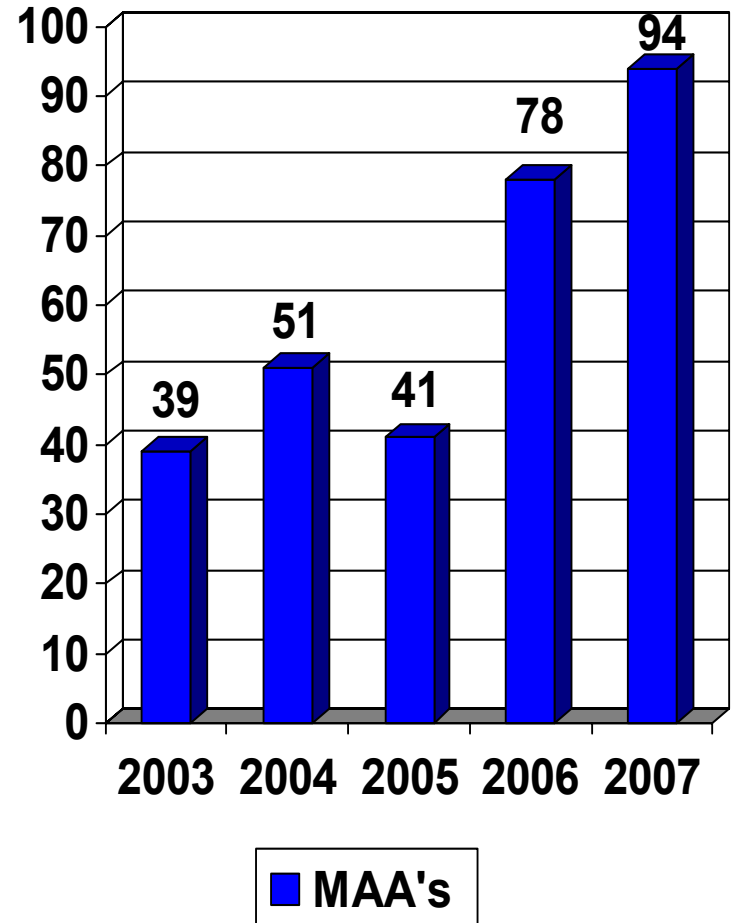
- Europe has approx 29% of total active global trials of 16,949
- FDA tracks 4887 USA trials in Europe
- 3,527 of these USA trials (72%) are at phase II & III status
- Represents a solid base from which future commercial QP and supply chain demand from USA into Europe will occur

Source: clinicaltrials.gov 2009

EU Market Opportunity



- A medicinal product may only be placed in the EU market when a Marketing Authorization Application (MAA) has been issued by the competent authority
- Increasing number of MAAs are being submitted to the EMEA
- Increasing the demand for professional support services in Europe



Source: EMEA, 2009

EU Market – overcoming challenges & addressing requirements



Professional **QP Services** are the critical first step to building an effective commercial supply chain in **Europe**

Regulatory Background



- Clinical Trial Directive implemented in May 2004
- Two primary routes for obtaining a licence for a commercial product in the EU:
 - *Centralized procedure*
 - *De-centralized procedure*
- All products imported into the EU must be released by a Qualified Person (QP)

Regulatory Considerations

- Identification of an EU Qualified Person operating under a Manufacturing Authorization
- Certification of “equivalence” to EU GMP’s at the sites of manufacture / packaging outside the EU
- Compliance with GMP as it applies to API’s (i.e. ICH Q7A) used in the imported drug product
- Identification of a site for removal of samples within EU
- Identification of EU laboratories in application (including contract laboratories)

Role of the Qualified Person



- Grounded in EU law –
(Article 51 of Directive 2001/83/EC)
- Each holder of a commercial manufacturing licence must name at least one person to act as a QP
- There are particular requirements for formal qualifications and practical experience
- QP is legally responsible for the release of commercial products into the EU market

OEU Product Requirements

1. Product must be received into EU – IP/EP
2. Samples removed for testing in EU
3. Country/region specific labelling/packaging (as applicable)
4. Every batch must be released by an EU QP and this can involve extensive reviews of:
 - Non EU manufacture & packaging batch record compliance with MAA
 - Deviations, OOS results or environmental failures from non-EU sites
 - Conditions of shipment
 - EU release test results

Quality Considerations



- QP audit of non- EU sites of manufacture/ packaging and EU contract analytical laboratories
- US company review of partners' compliance status
- Analytical transfer of release test methods
- Validation of shipping conditions to EU site(s)
- Potential for additional OOS results on completion of EU import testing
- Ongoing maintenance of arrangements *e.g. Product Quality Reviews, Customer Complaints, On-going stability monitoring*
- Technical Agreement defines responsibilities

Commercial Considerations

- Potential restrictions on utilisation of stock
- Multiplicity of packaging formats required for EU markets (i.e. leaflet, label & carton)
- Development of packaging artworks for EU countries
- Identification of distribution sites/partners within EU
- Range of contractual arrangements required
- Product pricing within the EU

Commercial Supply Requirements

CMO service
EU import testing <ul style="list-style-type: none"> ➤ Manufacturers import license ➤ CD licensed ➤ First site of EU import testing ➤ Stability testing
QP service <ul style="list-style-type: none"> ➤ Supplier auditing ➤ Full market release
Storage <ul style="list-style-type: none"> ➤ Controlled/ambient ➤ Refrigerated ➤ Frozen ➤ Secure vaulted (CD's)
Labelling & packaging <ul style="list-style-type: none"> ➤ Consultative services – pack design ➤ Artwork management ➤ Country specific labelling/packaging ➤ Small SKU handling
Distribution <ul style="list-style-type: none"> ➤ IP/EP management & customs clearance ➤ Courier/FF management

3PL/distribution services
Order management <ul style="list-style-type: none"> ➤ First contact to customers ➤ Maintenance of customer data ➤ Order receipt – phone, fax, e-mail, internet ➤ Multi-lingual ordering/queries ➤ Track and trace ➤ Invoice tracking
QP service <ul style="list-style-type: none"> ➤ Complaint management
Storage <ul style="list-style-type: none"> ➤ Returns handling
Financial management <ul style="list-style-type: none"> ➤ Consultative services – VAT, banking, incorporation requirements ➤ Invoicing ➤ Payment & collection ➤ Debtor management ➤ Dunning
Distribution <ul style="list-style-type: none"> ➤ Active management of carriers

Additional “services”
Order management <ul style="list-style-type: none"> ➤ Link to customer ERP system ➤ 24/7 service
QP service <ul style="list-style-type: none"> ➤ Active recall management (query)
Financial management <ul style="list-style-type: none"> ➤ Agent
Distribution <ul style="list-style-type: none"> ➤ 24/7 service ➤ Refrigerated pack design & validation ➤ Marketing information management
Labelling & packaging <ul style="list-style-type: none"> ➤ 24/7 service

Challenges



1. Complexity of supply chain partner identification
2. Contractual negotiations and breakdowns with partners
3. Failure to address diversity in national applications for EU Member States
4. Non-EU sites not inspection ready or critical findings on EU inspections
5. Poorly thought through EU business model and limited EU based commercial knowledge and data
6. Lack of suitably skilled and functionally experienced management
7. Under-estimation of project implementation resources
8. Little or no contingency planning for high risk ventures
9. Product launch timelines impacted by regulatory questions
10. Actual supply chain failures caused by real world events

Guidelines to Best Practice

- Remember - commercial EU launch involves moving into an environment of business uncertainty with many new variables
- Outsourcing key services is risky but is essential to get the job done
- Contingency planning is critical to success
 - Murphy's law usually applies
- Recognize that in Europe things are done differently and member state uniformity is not always the case
- Delays and mistakes are expensive and will substantially impact commercial launch plans
- Partnering with appropriately skilled and vetted service providers is more likely to generate success
- Getting it right first time is the best and only option

Best Practice – Must Do's

- Identify an EU partner to act as the site of release for imported product, prior to EU licence submission
- Complete key launch activities prior to EU inspection of US sites:
 - *Audit of site (s) of manufacture / packaging*
 - *Initiation of analytical method transfer activities*
 - *Drafting of Technical / Quality Agreement between the parties*
 - *Identify launch countries and initiate the commercial artwork process*
- Identify a supply chain solution for your launch countries, which can be expanded to cover other EU countries
- Consolidate any outsourced supply chain services with as few competent partners as can be found

Case study



EU “relaunch” of treatment for ACS (acute coronary syndrome)

- Transfer / Validation of Analytical Methods
- EU Import Analysis
- Design & Implementation of Stability programme
- Execution of Technical & Supply Agreements
- Licence Applications / Variations
- Selection of SKU / Market Breakdown
- Packaging Keyline Design & Fit tests
- Origination & Proofing of Packaging Materials
- EMEA Readability Trials
- Shipping Validations
- Design & Origination of Master Batch Documents
- QA/QP Audits of Primary Manufacturing Facilities



IQPC

QUESTIONS ?

SUBMITTING AN **MAA?**

