Regulatory
Quality
Compliance

Perspective on Global Regulatory Inspections

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Genentech

PMDA Presentation
Regulatory Agency Inspections of Genentech

- Genentech supports
  - The right of the patient to high quality, safe and effective drugs
  - Regulatory agency inspections of Genentech and its Contract Manufacturers (CMO)
    - Inspections should help control the risk to the patient and protect them
    - Sovereign government agencies may inspect Genentech provided there is a legal basis to do so.

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- Regulatory Agency Inspections Provide Value
  - Can be useful feedback on chemistry, manufacturing and controls with respect to current regulations
  - Calibrate current GMP compliance in comparison to other companies
  - Provide an independent scientific and/or regulatory perspective

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- Inspection Concerns
  - Increasing frequency of regulatory inspections in particular with emerging inspectorates/Rest of World (RoW)
  - Challenge to accommodate product specific inspections at sites manufacturing on a campaign basis
  - Potential conflicts with more than one inspection requested in the same time frame and inability to accommodate an inspection when requested
  - Inspection impact on manufacturing and quality operations

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- The number of Regulatory Agency Inspections is increasing

Genentech	2005	2006	2007
FDA	2	4	3
EMEA		2	
PMDA		1	2
RoW			
Mexico		2	*
ANVISA	2		
AEMPS		1	
Korea			1
Russia			*
California FDB			2
Genentech Totals	4	10	10

* Anticipated/proposed inspections

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- The number of Regulatory Agency Inspections is increasing (continued)

CMO	2005	2006	2007
FDA	3	4	6
EMEA	1	2	2
PMDA		1	
RoW			
Mexico		2	*
ANVISA		2	*
Taiwan BFDA		2	
CMO Totals	4	13	10

* Anticipated/proposed inspections

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- The number of Regulatory Agency Inspections is increasing (continued)

	2005	2006	2007
Genentech	4	10	10
CMO	4	13	10 - 15
Combined Totals	**8**	**23**	**20 - 25**

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- Inspection Concerns - Cost
  - Inspections consume a significant number of resources to prepare for, host, and follow up
    - Inspection Preparation
      - Document preparation
      - Facility walk-throughs
      - Advance request preparation
    - Logistics – scheduling, lodging, transportation, conference rooms, tours, meals, etc.
    - Inspection – participants and team members supporting the inspection
    - Follow-up and lessons learned
    - Responses to observations

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- Inspection Concerns - Cost (continued)
  - Typically over 100 people are involved in an inspection at Genentech
    - 1,000 to 2,500 person hours are consumed per inspection
    - This costs between $133,000 and $400,000 per inspection day
  - Total cost of inspections at Genentech (excluding the cost of any required corrective actions):
    - 2005 – $2,400,000
    - 2006 – $8,200,000

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- Inspections Concerns - Redundancy
  - Overall cost of essentially redundant inspections
    - Inspections are conducted very similarly by different agencies
    - Most inspectors are looking for the same information. The amount of detail may vary
      - Mexicans and Brazilians use check lists; other agencies rely on inspection guidance documents and training
  - Genentech is frequently being inspected to train inspectors about biotechnology (mostly RoW inspectorates)
    - We incur a risk of loss of intellectual property

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- Inspections Concerns - Unique Requirements
  - Regulators work locally and mandatory inspection and licensing requirements are unique
    - There is no global system of surveillance
    - Non-acceptance of observations from other inspectorates
    - There is insufficient mutual recognition of inspectorates globally
      - Results in an explosive increase in inspections and increased cost to the manufacturer
    - Duplicative, redundant inspections do not add value

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- Inspections Concerns - Unique Requirements (continued)
  - Unique inspections and licensing expectations will lead to country specific products
    - Multiple, unique specifications for the same product
    - Delays in product licensure
    - Results in higher product cost and delayed product availability to patients

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- Solutions Needed
  - Global system of surveillance
    - Mutual inspectorate recognition and acceptance of inspections
    - Expanded Mutual Recognition Agreements
    - Harmonization of inspection standards and cooperation between inspectorates
    - Protection of intellectual property

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- Solutions Needed (continued)
  - Globally accepted product specifications and no unique testing requirements leads to:
    - A decrease in the number of regulatory agency inspections by different inspectorates
    - Better intellectual property protection
    - No increase in product cost
    - No delay in licensure
    - Faster product availability to patients