

June 2011
EMA/705027/2010
Directorate

Interactions between the European Medicines Agency and U.S. Food and Drug Administration September 2009-September 2010

Introduction

The purpose of this document is to provide the first public annual update on the interactions between the EMA and the FDA under the confidentiality arrangements originally signed in 2003, as updated in 2010.¹ These arrangements provide for annual bilateral meetings between the FDA, the EMA and the European Commission to monitor the operation of bilateral activities within the scope of the agreed implementation plans. Since 2007, these bilateral meetings have also monitored the implementation of the Transatlantic Administrative Simplification (TAS) workshop deliverables as agreed in November 2007.² An update on the TAS activities was last published in October 2009.³ Due to the fact that the majority of TAS activities are now being addressed within the scope of the EMA-FDA confidentiality arrangements, it has been agreed that, following a final 2010 update report, further TAS updates will in the future be incorporated into this report which will be published annually, normally following a bilateral meeting.

This document has the added purpose of providing an opportunity for stakeholders to provide feedback to the EMA and FDA on these activities with a view towards ensuring that they are in line with agreed priorities and identifying appropriate performance measures.

It is important to clarify that this report is a snapshot of activities within the timeframe identified above. Many of the collaborative activities began during previous years, before a decision to have an annual public document was made, and most are ongoing activities. For further details please refer to the text of the overarching arrangements, the current implementation plan, or published updates in specific areas.

¹ [Background documents](#) concerning confidentiality arrangements and implementation plans and updates in specific areas can be found on the EMA website: and the [FDA website](#)

² http://ec.europa.eu/health/files/international/doc/eu_fda_action_plan_200806_en.pdf

³ http://ec.europa.eu/health/files/international/2009_tas_implementation_report.pdf

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Executive Summary

Following a significant increase between 2008 and 2009, ad hoc interactions between FDA and EMA have now stabilised to approximately 55 per month. Multilateral interactions involving FDA and EMA have increased, with regular trilateral Oncology teleconferences involving Health Canada, and the involvement of the Pharmaceuticals and Medical Devices Agency (PMDA) and Health Canada representatives in the paediatric cluster. A number of multilateral interactions on potential crises have also taken place involving WHO.

Significant efforts to streamline communication on crisis issues also were made, in particular communications on the contamination of Rotavirus vaccines and the review of rosiglitazone-containing medicines where there was significant media interest. Both agencies ensured they were dealing with the same body of information to assess overall benefit-risk. Synchronised, or near synchronised timing of announcements on both these high profile products took place.

A new Blood Products cluster was launched in February 2010 and initial discussions towards the establishment of clusters on Cardiovascular Products as well as one on Gastrointestinal Products have taken place.

In general, activities in all the clusters increased, and there was an overall increase in the number of ad-hoc requests for teleconferences on specific products and topics. Total interactions increased from an average of 50 per month in the first 6 months covered by this report, to about 55 per month between April and September 2010. Significant achievements within the clusters and interactions since the last bilateral include agreement on a single annual report format for orphan medicinal products⁴ and in the GCP area, the undertaking of 7 joint and 4 observational inspections. An interim report on the progress of the pilot of GMP inspections of Active Pharmaceutical Ingredient inspections (APIs) has also been published.⁵

The fact that a number of clusters are organised therapeutically while other clusters and interactions are potentially cross-cutting requires coordination to avoid duplication.

A large number of staff visits and exchanges also took place and there is now more routine involvement in the scientific work of both agencies. FDA representatives took part as observers in CHMP and SAG discussions on 4 products, and EMA representatives were provided with access to 8 webcasts of FDA Advisory Committees.

Liaison officials are now located in both agencies and these have been extremely beneficial from the perspective of education and timely communication. Tools for more effective tracking have been developed. The increase in overall interactions in the 12-month period from September 2009 to September 2010 has been driven in part by reaction to crises and in part by proactive measures to enhance EMA-FDA communication and collaboration now that both agencies have liaison officials in place.

Highlights September 2009- September 2010

- Liaison Placements now fully established in both agencies
- New Blood Products cluster set up
- Single annual report for Orphan Medicinal Products agreed
- Successful operation of GCP initiative with 7 joint inspections and 4 observed inspections performed
- FDA expert participation as observers in specific product related CHMP discussions
- EMA experts now routinely have access to FDA public meetings via webcasts

⁴ http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/03/WC500074890.pdf

⁵ http://www.ema.europa.eu/docs/en_GB/document_library/Report/2010/10/WC500097431.pdf

- Increase in uptake of parallel scientific advice
- Streamlined communication of several high profile products

Structure of report

This report loosely follows the structure of the current implementation plan and gives a brief overview of the key aspects of these interactions, highlighting the areas that work well and identifying areas that need further development, as well as some new opportunities that could be progressed.

The report does not repeat the background to the interactions in each area as these have been extensively addressed in previous documents outlining the concerned initiatives.

The report is organised as follows: regulatory cooperation (educational programme and staff exchanges), exchanges within the clusters and potential clusters (Oncology, Orphans, Paediatrics, Advanced Therapy Medicinal Products, Pharmacogenomics, Vaccines, Veterinary Medicinal Products, Blood Products, Cardiovascular and Gastrointestinal Products), pharmacovigilance/safety issues, inspections (including GMP and GCP pilot programmes), parallel scientific advice, nanotechnology and ad hoc exchanges, followed by a brief conclusion.

1. Regulatory Co-operation between EMA and US FDA

1.1. Continuation of the Educational Programme

There continues to be significant increase in activities related to this point, through staff exchanges, attendance at each other's meetings and in particular the appointment of specific liaison personnel. EMA colleagues attending an international meeting in Washington, June 2010 gave an overview of their activities to FDA at a town hall meeting open to all FDA staff on site and by broadcast. EMA also organised an international awareness training session, at which FDA's Liaison gave an overview of FDA's activities. She also gave an update on the Healthcare Reform legislation to the HMDE Unit. Informal meetings to explain FDA's organisational structure and oversight of clinical trials, as well as the approach to assessment of marketing authorisation applications, are common. EMA's Liaison has given presentations on EMA activities in the EU Regulatory network, the Centralised Procedure and Parallel Scientific Advice to several offices and divisions of the FDA (CDER, CBER and CVM).

Access to FDA advisory committees through webcasting facilities offered by FDA to EMA experts and staff has been found to be very helpful and increasing requests to observe these committees are made.

FDA representatives have participated by teleconference as observers at 4 meetings of the CHMP, and 4 Scientific Advisory Groups (SAGs), and at a workshop on strain selection for the next season influenza vaccine.

1.2. Staff Exchanges and visits

Since the last bilateral, approximately 20 FDA staff have visited the EMA and a similar number of EMA staff have visited the FDA (some more than once). This includes meetings by the Executive Director and senior EMA staff with key FDA staff in the margins of the international meetings as described above. It also includes EMA's concept of 'fellowships' where selected EMA staff spend a period of 2-3 weeks at FDA, observing meetings and developing contacts with staff in their respective areas of interest, where possible in conjunction with FDA's International Regulators Forum meetings hosted by the Center for Biologics Evaluation and Research (CBER) or the Center Drug for Evaluation and Research (CDER).

2. Interactions in areas identified as 'Clusters'

Specific areas, identified as 'clusters', have been identified in which regular exchanges take place.⁶ Those cluster-specific areas are Oncology, Orphans, Paediatrics, Advanced Therapy Medicinal Products, Pharmacogenomics, Vaccines and Veterinary Medicinal Products. A new 'Blood Products' cluster was created in February 2010, with a second teleconference scheduled for October 2010. Some initial discussions on the possibility of a Cardiovascular Products cluster and on a Gastrointestinal Products cluster also took place, with one exploratory teleconference taking place in each case

2.1. Oncology Medicinal Products Cluster

The cluster on Oncology is the longest standing cluster (since 2004) and continues to meet at approximately monthly intervals, with meetings lasting 1 to 1.5 hours. Dedicated contact points have been established on both sides and there is agreement on agendas and background documents one week before the teleconference. Concerned Rapporteurs and relevant EMA staff participate for their respective products on the EMA side, with reviewers from FDA's Office of Oncology on the FDA side.

Between September 2009 and September 2010, 8 routine teleconferences took place including one product specific teleconference. On average, 2-7 products are discussed with 3-6 included for information. The Agenda also includes an overview of Scientific Advice requests which can be sub-divided into 7-10 final Scientific Advice letters and 10-15 ongoing procedures.

In June 2009, following finalisation of EMA and Health Canada's implementation plan, a first successful trilateral teleconference between EMA/FDA and Health Canada was held on a specific product of mutual interest. Health Canada representatives have participated routinely since the end of 2009 in the cluster teleconferences and have taken on a more active role since June 2010, with the opportunity to propose agenda topics.

Product specific discussions are being held more and more also during initial stages of the scientific assessment (before the end of the first round of assessment), providing a platform for discussions between rapporteur teams and international colleagues early in the procedure. Advance notification on product related discussions at upcoming scientific meetings is also a feature of the interactions.

2.2. Orphan Medicinal Products Cluster

A major achievement announced in February 2010 was the agreement on the acceptance of a common annual report and a common submission day, allowing companies to submit a single annual report which can be assessed by both FDA and EMA.⁷ This involved an additional number of teleconferences and exchange of information to discuss timing and specific aspects of the project.

A second important achievement during the period was an agreement to include discussions on monthly exchange of submissions for orphan designation to both agencies.

A total of 7 periodic teleconferences on Orphan Medicinal Products took place between September 2009 and September 2010.

At these meetings, the discussion usually includes possible agreement on common projects and sharing of information on difficult applications submitted in order to approach/harmonise, as far as possible, criteria for designation. Since the start of 2010, discussions have also included analysis of divergent opinions and discussion of specific cases, as well as analysis of common applications submitted to both agencies.

⁶ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500017981.pdf

⁷ http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/03/WC500074890.pdf

In addition, there were two teleconferences on specific topics: supply problems from a specific orphan manufacturer and a brainstorming meeting about an FDA proposal to explore alternative pathways for orphan designation.

2.3. Paediatric Medicinal Product Cluster

The cluster on paediatrics is also very successful and interactions continue to be fruitful on both sides.⁸ Monthly teleconferences are held between EMA's paediatric team and the FDA: these conferences are coordinated by the FDA Office of Pediatric Therapeutics (OPT). Members from other FDA offices or divisions regularly participate. From September 2009 until September 2010, 42 products and 4 general topics were discussed during a total of 9 regular teleconferences.

During these conferences Paediatric Investigational Plans (PIPs) are discussed in detail and information between the two agencies are exchanged. In addition, more general questions have also been addressed, such as types of studies for glioma, extrapolation and choice of endpoint for pulmonary arterial hypertension, safety of proton pump inhibitors and patient/parent reported outcomes.

A representative from Japan's PMDA continues to participate as an observer, and a representative from Health Canada joined as an observer in September 2010.

Several follow-up telephone meetings outside of the monthly teleconferences have also been organised.

At the end of 2009, FDA staff started participating in the meetings of the Paediatric Committee (PDCO) Non-Clinical Working Group and its Formulation Working Group.

EMA has provided access to FDA colleagues to its internal database which includes scientific details of all PIPs.

Staff exchanges continue, with visits of three EMA staff members to OPT in 2010, including being given the opportunity to listen in to the PeRC, and visits of FDA OPT staff to observe some of the activities of the EMA, including the PDCO meetings.

2.4. Advanced Therapy Medicinal Products Cluster

Cluster teleconferences take place on a bi-monthly basis, in the margins of the Committee for Advanced Therapies (CAT) meetings. The agenda of such teleconferences are agreed jointly between FDA and EMA on basis of the discussions at the CAT (CAT table of decisions shared with FDA) and the FDA Regulatory activities (overview document received from FDA). An average of 2-3 products are discussed and 1-2 guidance documents or general topics.

Following the successful visit of two FDA staff from the Office of Cellular, Tissue, and Gene Therapies (OCTGT) in 2009, FDA colleagues participated at an EMA organised Workshop on stem cell medicinal products in May 2010, and subsequently attended the CAT meeting which took place on the following day.

An EMA staff member from the CAT secretariat will visit FDA/CBER/OCTGT in November 2010.

2.5. Pharmacogenomics Cluster

Quarterly cluster meetings take place by teleconference in this area in accordance with the guiding principles agreed in 2006 on Processing Joint FDA EMEA Voluntary Genomic Data Submissions (VGDSs).⁹ From September

⁸ The Principles of Paediatrics Interactions can be found at

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500017969.pdf

⁹ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500017982.pdf

2009 to September 2010, interactions between FDA and EMA were reinforced through 4 joint company briefing meetings, as well as through discussions on 2 product-specific genomic biomarkers, 3 draft EMA guidelines, and 1 draft FDA guideline.

Discussions on the revision of the operation of joint briefing meetings are also ongoing, since it is recognised that not all discussions are strictly speaking 'pharmacogenomic' and new methodological approaches are also included. The concept of Voluntary exploratory Data Submission (**VXDS**) meetings is under review.

The relevant FDA and EMA leads have arranged face-to-face participation in each other agencies' meetings.

2.6. Vaccine Cluster

Formal Vaccine cluster meetings between September 2009 and September 2010 were (due to the need for heightened communication during the pandemic) replaced by timely exchange of information on pandemic vaccines, with the major focus being on the exchange of post-authorisation data. Both agencies continued to participate in bi-weekly WHO organised meetings on surveillance for Guillain-Barré syndrome (GBS). FDA participated at a serology workshop organised by EMA and at a workshop on strain selection for the next seasonal influenza vaccine.

Exchanges of note in the pandemic area related to a suspected problem with stability of certain pandemic vaccines, suspected safety signals on anaphylaxis and on narcolepsy, and reviews related to ongoing post-authorisation experience.

Similarly, a series of interactions on Rotavirus vaccines began with notice of publication of new test results which showed possible viral contamination of a number of vaccines including Rotavirus vaccines in March 2010. Efforts to share scientific approaches and to streamline communication were made. FDA's public meeting on Rotarix findings, the testing approach, and the broader implications, was attended by EMA staff and made available to EMA via webcast.

Agreement to work together with WHO on the implications of this testing approach on the quality and safety of other vaccines and biological products was reached.

A possible intussusception safety signal arising from new studies on one of the Rotavirus vaccines was also discussed on a bilateral basis and with WHO representatives.

Informal collaboration on scientific advice on three 'advanced therapy' oncologic vaccines also took place.

2.7. Veterinary Medicinal Products Cluster

Cooperation between the EMA and the CVM in the context of the Veterinary Medicines cluster continues to be excellent.¹⁰ Both parties have expressed satisfaction with the current operation of the arrangements and strive for continuous improvement. In addition to regular, scheduled quarterly bilaterals (via video or teleconference) there have been fruitful ad hoc exchanges of information on a variety of topics of mutual interest. FDA Veterinary cluster participants visited EMA colleagues in person for one such exchange. Likewise, EMA veterinary staff have visited with FDA in the margins of other US meetings. In addition Working Groups may be set up on specific subjects and/or ad hoc meetings may be organised following the request of one of the two parties. In many cases, each specific issue, (e.g. marketing authorisation of a specific product) is subsequently discussed outside the context of formal meetings through bilateral exchanges of information and documents.

In general, the Agenda includes following topics:

¹⁰ The Implementation Procedures for Veterinary Medicinal Products Cluster can be found at the following location: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500017956.pdf and Principles for Parallel Scientific Advice can be found at http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500017960.pdf

- Current and future applications for MA, SA and MRLs
- Guidelines Review and other regulatory activities:
- VICH Issues
- Safety Issues
- Pharmacovigilance information

In addition to such meetings, the following, non-exhaustive list of topics have been addressed in ad-hoc exchanges during 2009-2010:

- MRL applications for specific substances
- Product specific issues
- Codex/CCRVDf documents and guidelines
- Antimicrobial resistance
- Cooperation in the VICH Outreach Programme
- Queries on safety, efficacy, adverse drug reactions and pharmacovigilance/conditions of use of specific products, particularly novel technologies being introduced for the first time to veterinary medicine

Relevant members of Agency staff participate in the meetings/videoconferences depending on the subject discussed. In discussion of scientific topics, experts from CVMP and/or Scientific Working Groups may be invited to join the meeting. Discussions have now started, including during an EMA staff visit to FDA, with the aim to extend to the veterinary area the greater cooperation on inspections of manufacturers of products and active ingredients that is taking place in the human area.

2.8. Establishment of new Blood Products Cluster

Following agreement to establish this cluster at the last bilateral meeting, the first kick-off meeting of this new cluster was held in February 2010 in the margins of the CHMP's Blood Product Working Party meeting. A second teleconference was scheduled for October 2010.

At the first meeting by teleconference, a number of areas of mutual interest were identified including exchange of information on draft guidelines of mutual interest, exchange of urgent information on safety issues, discussions on ongoing applications, scientific advice, upcoming meetings and workshops, etc. Specific issues that will be addressed include the following: Clinical validation studies and labelling content for paediatric indications (factors VIII and IX), Clinical trial design for long lasting products (modified plasma derivative analogues), Study requirements for Hepatitis B Immunoglobulin, differences between US and EMA approaches regarding potency assays, and discussion of databases held by EMA and FDA.

3. Requests to establish additional Clusters

In addition to the establishment of the new cluster on Blood Products, initial discussions towards the establishment of clusters on Cardiovascular Products as well as Gastrointestinal Products took place. For the latter two, both agencies are committed to advancing exchanges of scientific information in these important therapeutic areas, taking into account the respective organisational structures.

3.1. Interactions on Gastrointestinal (GI) Products

At the request of FDA, an initial teleconference on Gastrointestinal Products took place on January 19 2010. Although the interactions during this teleconference were useful, the topics addressed did not come within the

scope of the section responsible for gastrointestinal products in the EMA and it is expected that the majority of interactions will be organised on an ad-hoc basis.

3.2. Interactions on Cardiovascular Products

An initial teleconference took place in May 2010 and a second one was planned for October 2010. Three specific products were discussed, and EMA provided the relevant assessment reports. Experts from both sides had a chance to meet during an externally organised Workshop in Luxemburg in December 2009.

Both sides believe that there is scope to develop this into a successfully functioning cluster.

4. Interactions on Pharmacovigilance/safety issues

Although not defined as a cluster, interactions in the area of safety continue to play an important part in the ongoing collaboration between FDA and EMA. Bilateral videoconferences involving the CHMP Pharmacovigilance working party take place on a bimonthly basis and include product related issues and issues related to risk management. Usually 5-6 products are discussed at these teleconferences.

These are complemented by regular informal teleconferences (e.g. before the CHMP meeting), in order to exchange information on emerging safety and strategic issues.

EMA shares the 'Early Notification System' (ENS) introduced in 2008 on a monthly basis, and feedback continues to be positive. On the FDA side advance notice of publication of its quarterly update reports on potential safety signals are regularly received. In addition FDA provided advance notice on approximately 20 product related matters and forthcoming publications.

A dedicated teleconference with FDA in September 2010 to learn about FDA actions in follow-up to their public hearing on use of the internet for collecting adverse reaction reports took place.

Additional collaboration on pharmacovigilance takes place in the context of the IMI PROTECT and FDA Sentinel projects. FDA's Office of Safety director is a member of the IMI PROTECT External Advisory Board and has participated in two External Advisory Board meetings. Three Sentinel/ENCePP-IMI teleconferences with the FDA took place, two in 2009 and one in 2010. In addition, there was a 1-day multilateral meeting in Washington in June 2010, in the margins of DIA 2010, to discuss the various collaborative projects (Sentinel, OMOP, ENCePP, PROTECT, DSEN, EU-ADR, etc) which was attended by EMA staff in person and by teleconference.

There have also been various teleconferences under IMI PROTECT to discuss a specific project on observational medical outcomes (OMOP).

Additional collaborative projects of note include a joint project on Progressive Multifocal Leucoencephalopathy (PML) Research Agenda to stimulate research into this important safety issue that affects some biological agents and the co-authoring of related publications.

5. Interactions in the Area of Inspections

Since 2008, regular interactions in the area of inspections have mainly been organised within the framework of specific pilot initiatives on GMP and GCP as described below. Ad hoc exchanges on specific products, quality defects, product shortages and on draft guidelines also take place.

5.1. GMP Pilots

The main focus of EMA-FDA interactions in the area of GMP inspections in the period September 2009-September 2010 related to the Active Pharmaceutical Ingredient (API) pilot project initiated in 2008 (in cooperation with the European Directorate for the Quality of Medicine and the Therapeutic Goods

Agency/Australia),¹¹ and the EMA-FDA pilot on cooperation on Finished Product inspections in the context of the Transatlantic Administrative Simplification workshop deliverables. The objective of the API pilot is the sharing of information on API inspections in 3rd countries to enable more efficient use of inspection resources and greater inspection coverage. The joint inspections Finished Products pilot between EMA and FDA/CDER aims to develop ways of working together on joint inspections of routinely-scheduled sites in the territory of USA or EU, to reduce duplicate inspections and resultant burden on both industry and the agencies.

These projects provide a need for regular interactions, exchanges, teleconferences, and face-to face meetings.

An interim report on the API pilot has now been published¹² which provides some statistics and formally communicates agreement of all participants to extend the project duration by 6 months to the end of the calendar year 2010. The extension was mainly to allow a better measure of the success, or otherwise, of the project due to some delays in starting the practical phase of the project. The project is currently running well and its success means that collaboration with FDA in this area is likely to continue after the project formally ends. The report illustrates the extensive exchange of API inspection plans and inspection reports, leading to increased transparency in inspections performed by participating authorities, as well as to an increase in number of inspections which are of value to more than one authority.

According to the interim report, 1046 site entries were provided by the pilot participants in the 'Master List'. European agencies submitted 499 sites and FDA submitted 352 sites, of which 38% and 54% respectively were shared with other pilot participants (i.e. sites of interest to more than one regulatory authority). The 8 joint API inspections conducted which are referred to (4 in India, 1 in Croatia, 1 in Mexico, 1 in Japan and 1 in China) have also lead to a reduction in duplicate inspections and have facilitated better use of our combined inspectional resources.

In addition, 114 inspection reports have been requested between the pilot participants, of which 20 European reports were requested by FDA and 47 FDA reports by Europe..

CVM has also expressed an interest in collaboration on GMP matters in the veterinary area and discussions have commenced.

With respect to the pilot on Finished Products, further opportunities for pre-authorisation inspection collaboration beyond the 2 joint inspections already performed in 2009 have proved elusive. Challenges such as the need for simultaneous submissions to both Agencies; the restriction to non-biological products with manufacturing sites in US or EU which trigger pre-authorisation inspections of similar scope. Inspection plans are being exchanged and planning for possible joint routine/surveillance inspections is currently ongoing.

A reminder about the finished product inspection collaboration was published on the EMA website in August 2010, inviting companies to participate in the pilot programme¹³ for upcoming FDA or EMA pre-approval or routine/surveillance inspections.

5.2. GCP Pilot

The Joint GCP initiative launched in September 2009 has been particularly successful. One of its aims is to reinforce and systematise periodic information exchanges on GCP-Related Activities between FDA- initially CDER- and EMA. These include the exchange of GCP inspection plans to ensure the selection of studies and sites is well informed, and inspection coverage is improved, the exchange of information on applications submitted to help identify candidates for collaborative inspections, and the exchange of inspection outcomes and reports (negative and positive) and their potential impact, where the clinical trials and/or inspected sites/organisations are of common interest.

¹¹ http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500005014.pdf

¹² http://www.ema.europa.eu/docs/en_GB/document_library/Report/2010/10/WC500097431.pdf

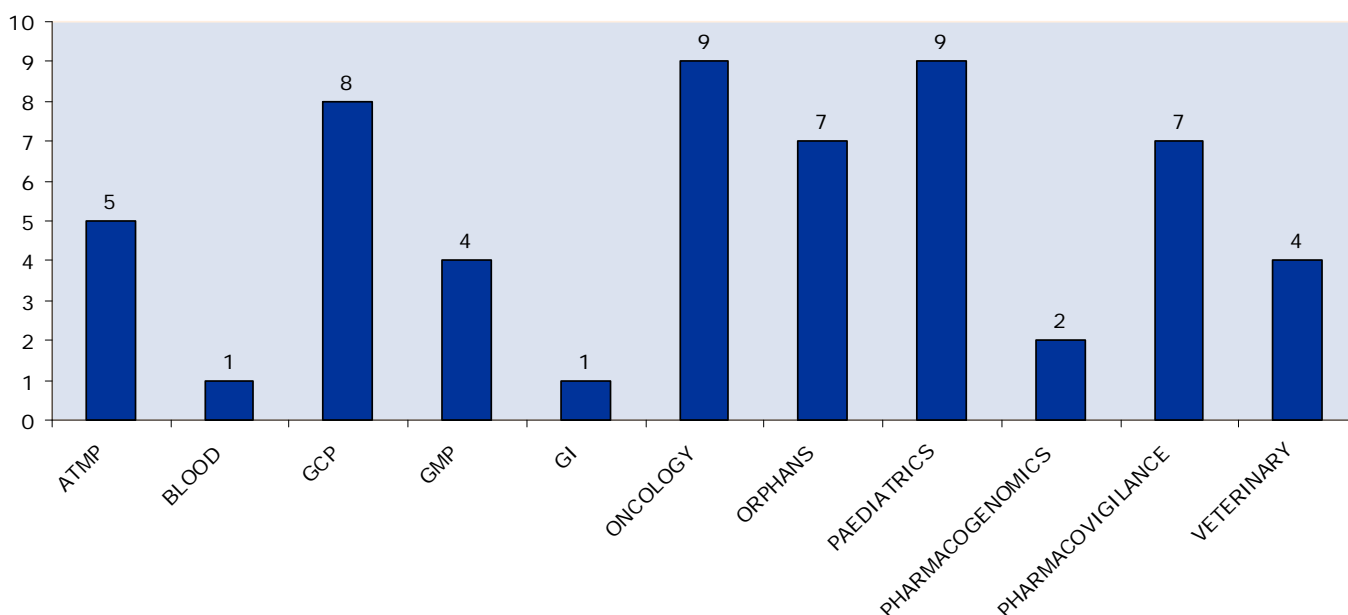
¹³ http://www.ema.europa.eu/docs/en_GB/document_library/Report/2010/11/WC500098836.pdf

The goals also include the conduct of collaborative GCP Inspections, in particular joint and observational inspections, and the sharing of information on interpretation of GCP (draft guidelines, policies, etc. on GCP matters).

As of September 2010, 14 teleconferences have taken place, of which 6 have been product-specific and two face-to-face meetings in the margins of international conferences.

7 joint and 4 observational inspections (relating to three products) have been performed and GCP related information has been exchanged on more than 30 products. In addition exchanges of views on interpretation of GCP documents have been organised on 7 occasions.

Number of regular interactions between EMA and FDA Sept 2009-Sept 2010



6. Parallel Scientific Advice

Following a period of relatively little action, activities on parallel scientific advice have increased significantly.¹⁴ There have been 7 Parallel Scientific Advice requests in the period of September 2009-September 2010. In 2010, three parallel Scientific Advice procedures have been completed up to now. Letters of Intent for three more parallel Scientific Advice (PSA) procedures have been received and accepted by both agencies. The scope of the products for which sponsors are requesting PSA is widening, both in terms of therapeutic areas and innovative nature and complexity of the specific products.

7. Nanotechnology

Following the international nanotechnology conference organised by FDA in June 2009, it was agreed that the issues prompted by applications of nanotechnology require two levels and forums of international coordination:

- One at high (political) level concerning the general oversight and sharing of information on main regulatory actions possibly triggered in specific areas

¹⁴ EMA-FDA Parallel Scientific Advice 'General Principles' for human medicinal products http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/11/WC500014868.pdf and for veterinary products http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/12/WC500017960.pdf

- One at technical level addressing the specific scientific issues identified in specific areas.

It was also recognised that there are scientific aspects that may be common and have regulatory implications across areas (e.g. definition issues and borderline products).

EMA has taken the lead on the scientific and technical aspects in the nanopharmaceuticals area, organising an international workshop on September 2, 2010.¹⁵ In collaboration with day 2 of this 1st International Workshop on Nanomedicines at the EMA, the FDA lead made a presentation entitled, 'An FDA Perspective on Nanomedicines: Current initiatives in the US.'

8. International standardisation activities

Extensive discussions, visits, and meetings between FDA and EMA staff have taken place to progress the maintenance of the Identification of Medicinal Products (IDMP) project.

9. Miscellaneous

Discussions between the EMA sector responsible for interactions with patient and health care professionals and staff from FDA's Patient representative programme took place in November 2009.

Discussions on combination products at an FDA-hosted quintilateral meeting held in April 2010.

EMA hosted a representative from FDA's Office of Combination Products in September 2010.

Exchanges to develop a pilot on exchange of assessment information on applications including elements of Quality by Design (QbD) are ongoing.

A discussion took place in January 2010 on approaches to comparability protocols.

A teleconference between EMA's SME office and FDA's small business team took place in September 2010, exploring opportunities for collaboration.

10. Routine Exchanges

10.1. EMA to FDA Exchanges

- FDA is included in the Early Notification System prior to monthly CHMP meetings. FDA also receives communications following every CHMP meeting.
- EMA has provided FDA with a list of planned GMP (finished product) inspections
- EMA provides FDA with a listing of planned applications and planned GCP inspections within the GCP initiative.
- Extensive exchanges of information on planned and performed GMP inspections of APIs master list take place within routine teleconferences.

10.2. FDA to EMA Exchanges

- FDA provides EMA with the Advance notice of the FDA's post authorisation adverse event postings. In addition, FDA began sharing a new type of quarterly report in 2010 for newly authorised products since September 2007. This latter summary of FDA's assessment of the new drug's safety 18 months post approval, or after 10,000 patients' exposure, whichever is later, and takes into account multiple sources.

¹⁵[European Medicines Agency's workshop on nanomedicines background documents](#)

- FDA sends advance notification to EMA of extracts from AERS (Advance Event Reporting System).
- FDA provides EMA with CBER quarterly reports on GCP inspections.
- FDA provides EMA with a listing of planned GCP inspections within the GCP initiative.
- Extensive exchanges of information on planned and performed GMP inspections of APIs master list take place within routine teleconferences.

11. Ad Hoc Exchanges

The total number of monthly FDA-EMA interactions (teleconferences, document exchanges, cluster interactions, pilots, and face-to-face encounters) is now an average of about 55 per month, excluding document exchanges relating to cluster and pilot activities..

Apart from the routine exchanges in the clusters identified, the majority of exchanges have been ad hoc exchanges on safety issues and specific products and continuation of issues relating to the pandemic crisis (Stability issues, review of potential signals. For the period from September 2009 to September 2010, there were more than 200 ad-hoc product related exchanges (teleconferences and document exchanges).

Of the 100 or so teleconferences organised during the reporting period, about 50% of them related to ad-hoc product issues not covered within the routine cluster or pilot activities.

Specific product related discussions serve to greatly increase understanding of the issues and intended actions on both sides. From the EMA and FDA perspective, these interactions have also helped in the preparation of external communication activities.

Some difficulties in finding suitable times for discussions have been encountered, and exchanges are greatly facilitated when there is a clear and detailed list of issues for discussion on both sides. Where exchanges are non-urgent, the possibility of providing written responses should always be considered.

Conclusion

The period of September 2009 to September 2010 was a time of consolidation for FDA-EMA interactions in most areas. Following a significant increase between 2008 and 2009, interactions between FDA and EMA stabilised to approximately 55 per month. There is an increasing trend towards multilateral interactions involving FDA and EMA and other regulatory authorities.

In general, activities in all the clusters and pilots increased, and there was an overall increase in the number of ad-hoc requests for teleconferences on specific products and topics.

A large number of staff visits and exchanges took place, with increasing routine involvement in the scientific work of both agencies. FDA representatives took part as observers in CHMP and SAG discussions, and EMA representatives are regularly provided with access to webcasts of FDA Advisory Committees.

Liaison officials are now located in both agencies and these have been extremely beneficial from the perspective of education, awareness of interaction opportunities and timely communication. Tools for more effective tracking have been developed.

Deliverables identified as part of Transatlantic Administrative Simplification Workshop are now firmly integrated into regular activities between the Agencies.

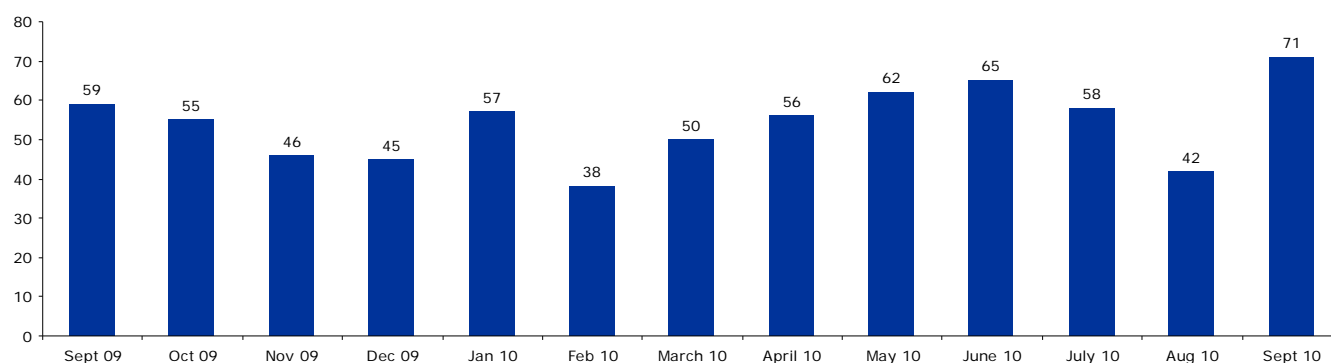
The consolidation of communication and collaboration mechanisms between FDA and EMA continues to be an important tool in addressing public health issues related to medicines and in increasing efforts to learn from each others' approaches as well as avoiding duplication and facilitating synergistic activities.

ANNEX I – Statistics on EMA-FDA interactions

Total number of monthly interactions Sept 2009 – Sept 2010

(excluding individual document exchanges in Paediatric cluster, Oncology cluster, GMP and GCP pilots)

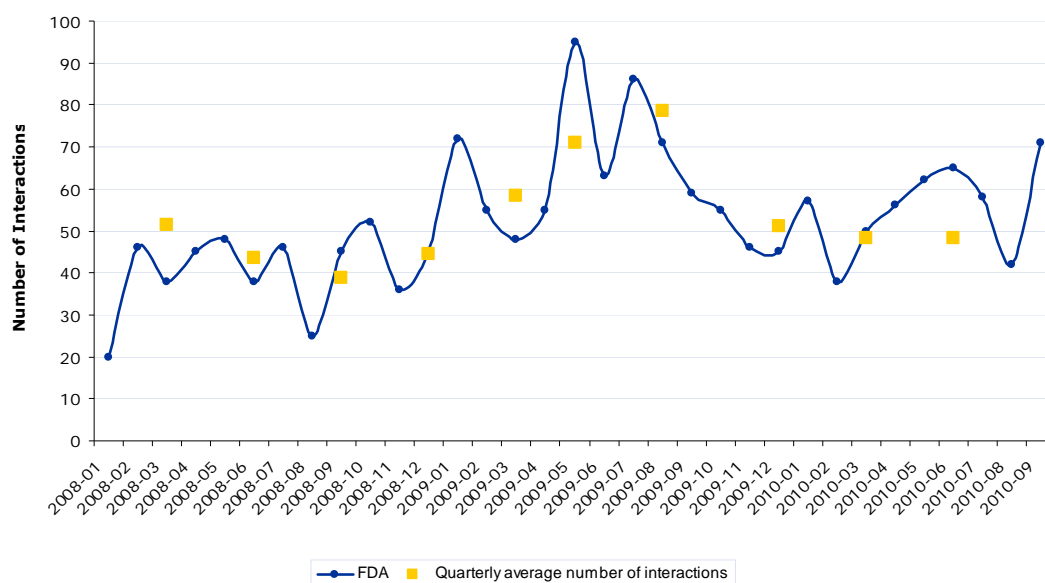
Number of EMA-FDA Interactions



Total number of monthly interactions January 2008 – Sept 2010

(excluding individual document exchanges in Paediatric cluster, Oncology cluster, GMP and GCP pilots)

FDA-EMA Interactions January 2008-September 2010



Annex 2: Table of Abbreviations used

Abbreviation	Full Text
API	Active Pharmaceutical Ingredient
ATMP	Advanced Therapy Medicinal Product
CAT	Committee for Advanced Therapies
CBER	Center for Biologics Evaluation and Research
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Foods
CDER	Centre for Drug Evaluation and Research
CHMP	Committee for Medicinal Products for Human Use
Codex Alimentarius	A collection of internationally recognised standards, codes of practice, guidelines and other recommendations relating to foods, food production and food safety.
CVM	Centre for Veterinary Medicine
CVMP	Committee for Medicinal Products for Veterinary Use
DSEN	Drug Safety and Effectiveness Network
EMA	European Medicines Agency
ENS	Early Notification System
FDA	Food and Drug Administration
GBS	Guillain-Barré syndrome
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
HBIg	Hepatitis B Immune Globulin
IDMP	Identification of Medicinal Products
IMI	Innovative Medicines Initiative
MRL	Maximum Residue Level
OCTGT	Office of Cellular, Tissue, and Gene Therapies
OMOP	Observational medical outcomes
OPT	Office of Pediatric Therapeutics
PDCO	European Medicines Agency Paediatric Committee
PeRC	Pediatric Review Committee
PIP	Paediatric Investigation Plan

Abbreviation	Full Text
PMDA	Pharmaceuticals and Medical Devices Agency (Japan)
PML	Progressive Multifocal Leukoencephalopathy
QbD	Quality by Design
SAG	Scientific Advisory Group
SME	Small and Medium-sized Enterprises
VGDS	Voluntary Genomic Data Submissions
VxDS	Voluntary exploratory Data Submission
WHO	World Health Organisation