When a product's quality is divided into design quality and manufacturing quality that related to manufacturing quality becomes the target of Change Control in the GMP. At that time, in order to assess the impact of a change on quality and the validity of that change, the impact on design quality obtained during the development stage, i.e., the quality suited for the targeted use, should also be considered. It is a principle that basic design quality does not change before versus after the change in its target use and use method. Therefore, the quality of a product after the change should be evaluated cautiously, taking the design quality into consideration. Non-voluntary changes in design quality should be avoided, i.e. change should be evaluated cautiously for whether it is suitable for the targeted product use prior to implementation of the change.

In evaluating the impact on quality, at least, verification of compliance with approved specifications is required, but when there is concern that the potential impact on design quality, multi-faceted evaluation and analysis should be considered not only for specifications and testing methods but also for product characteristics appropriately related to the design quality according to the content of the change or the product characteristics.

In order to perform appropriate change control in the GMP, therefore, it is necessary to accumulate and maintain technology information related to design quality which is the background of product quality assurance. The scope and document form of this information should be defined in accordance with the characteristics of individual products, based on the results of technology transfer of not only manufacturers who are entities implementing the GMP but also marketing approval holders or on others.

6．Risk Management for Changes

With Change Control, appropriate risk management should be implemented in consideration of technology documents related to design quality, understanding of processes and actual results of manufacturing quality and the latest manufacturing science, extending from the drafting and policy decision stage of an individual change to the effectiveness confirmation of that change and product release.

At that time, the impact of the change on product quality should be assessed sufficiently. More specifically, the following must be confirmed: the degree of the impact on the appropriateness of targeted product use and the quality permissible for provision to the market as a product suited for the targeted use which is maintained even after the change.

"Risk" means a deviation from the established or expected results, and when evaluating the degree of impact, it is required that the impact be recognized as clearly occurring regardless of whether there is acceptance or rejection of a change or whether that change is large or small in terms of the degree of impact. Assessment is an evaluation of the degree of magnitude of changes of this type. It should be kept in mind

that assessing existence or non-existence of risk is not the objective of Risk Assessment

For the details of Risk Management and Risk Assessment, refer to "Guidelines for Quality Risk Management", Ministerial Notification No.0901004 by Director, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MLHW, dated September 1, 2006,.

6．1 Risk Assessment

For Change Control, appropriate Risk Assessment should be implemented in consideration of technology documents related to design quality, understanding of processes and actual results of manufacturing quality, and the latest manufacturing science, during the early stage of drafting and policy approval etc. of individual changes. At that time, it is possible to use actual performance results and experience obtained in implementing past changes on the same or similar products.

In the Risk Assessment implemented prior to a change, the degree of potential impact of the change on quality should be evaluated.

For example, when implementing a change that is intended to improve the manufacturing process for, for example, process stabilization or to improve items related to quality control from the aspect of preventing deviation, consider doing a Risk Assessment at the poly-decision stage for deciding whether "a change that can be a preventive measure should be implemented immediately", or "it should be implemented after observation of the time course of corrective actions for a certain period", by taking the content of corrective actions into consideration. Then, at the stage of creating a concrete plan after the policy for implementing the change is decided, another Risk Assessment becomes necessary at an aspect different from the policy-panning stage. At the stage of consideration of this concrete plan, when multiple technical methods are presented, it is possible to decide by using selection methods such as FMEA (Failure Mode and Effect Analysis) etc. Before making a judgment, evaluations from the aspects of"whether a change is effective to reduce risk" and "whether it is possible to consider results of a change to lead to secondary problems" will also required.

Where knowledge etc. based on past data and similar products is not considered to be adequate for implementing Risk Assessment, the impacts on quality of the said change should be assessed in advance by test manufacturing, etc. It is possible to choose from newly-established experimental methods of appropriate scale, test evaluation in actual manufacturing equipment or others, depending on the contents of the change, taking product characteristics and development progress into consideration.

After creating a concrete plan and completing a change plan document, the next step is review of the change implementation plan, and it is required that the document for the change plan contains information which will be used to decide the severity of the verification on the impacts on quality which will occur when the change is actually implemented, and whether or not validation is necessary, depending on the magnitude of

risk related to the change. Therefore, the Risk Assessment result needs to contain methods for monitoring and for verification, etc. for risk occurrence during the change implementation in addition to the identification of risks and evaluation of impacts on quality.

In addition, when the impact of a change on quality is assessed as possibly extending to the following as a result of Risk Assessment, it is not possible to draw a conclusion based on a single evaluation done within a GMP organization, and evaluations/studies of a higher level, involving efficacy, safety, for the implementation of the change, from the aspects of product quality assurance, are required.

- When the impact of the change on product quality cannot be evaluated by established testing/analytical methods, standards, etc.
- When efficacy and safety evaluations, such as additional clinical studies, are needed because something different from already approved matters is revealed.
- When toxicity studies, etc. for the confirmation of the safety of new impurities, are needed in order to evaluate the impact of a change.
- When additional clinical studies etc., for the evaluation of impacts due to a significant change in the drug formulation, are needed.

As noted above, there are opportunities for implementing Risk Assessment differently at various stages of quality evaluation beginning from policy making, drafting of changes in plans, with all thought given to evaluation of the quality of the change. However, risk is so specific to respective products and manufacturing lines that individual risks need to be assessed multi-dimensionally through multiple views, considering the risk variation according to life-cycle when evaluating the impact on quality.

Since an evaluation needs to be done from multidimensional aspects, it should not be limited to the quality and manufacturing units but also to examining equipment/facility control, engineering, raw materials procurement, production planning, research and development, pharmaceutical affairs regulations, and delivery(marketing) etc., where appropriate depending on the content of the change. Persons responsible for these sections or functions should perform Risk Assessment from their own viewpoint and at their own responsibility, according to the contents of the change.

One probable example would be in Risk Assessment at the stage of deciding proposal/implementation policy, manufacturing, quality control, engineering, research and development and pharmaceutical affairs regulations; and at the stage of selecting a concrete change plan, responsible persons working in the sections related to the assessment or who perform certain functions in the assessment are appointed to be involved in Risk Assessment, depending on the intricacy of technological evaluation or follow-up tracking procedures considered necessary in the practical process of change.
It does not necessarily mean participation as an organization, but individuals or multiple

people in charge who can manage necessary functions are allowed. The important point is to make Risk Assessment effective by recruiting the necessary personnel resources, assigning responsibilities, and establishing procedures.

6．2 Risk Assessment and Classification of Change

Classification of Change depending on the degree of risk is useful for Risk Management because differences occasionally occur, depending on the magnitude of extracted risks, in advance communication to a market approval holder, in verification items, which are established prior to implementation in the process where the change is implemented, and in procedures and methods for monitoring control of the process. The classification should be done in a manner that makes it possible to share an understanding of evaluation results: "it has an impact on quality" from the aspects of scientific technology. For example, it is possible to define it thus: "it has an impact on quality" means that a change in quality characteristics becomes apparent, while "it has no impact on quality" means that a change in quality characteristics is very small, or it does not contribute to the change in quality characteristics. Companies are considered to possess/accumulate data and information on factors in the process and equipment that affect quality characteristics and the degrees of occurrence of change in characteristics of quality such as a knowledge of design and manufacturing quality; and based upon such knowledge, it will become possible to estimate what changes are brought about by changes in processes or equipment. The quality change produced by a change is not zero. Thus, based on recognition that a change is equivocal, it is possible to consider that, in the GMP, the classification is an index for the particularity and rigidity of quality evaluation and the effectiveness confirmation done before versus after change.

From these aspects, the classification could be a tool for estimation of requisite resources at the time of an acceptance/rejection judgment of a change or implementing the change in consideration of the magnitude of impacts on quality based on the results of assessment. Furthermore, for marketing approval holders, it is useful for judging the impact on the market and the necessity of legal procedures for the descriptions in their approval letters, and is also useful as a tool facilitating negotiations with manufacturers. Meanwhile, care must be taken because there is a potential for a risk to be overlooked by a single-meaning, mechanical classification of risks.

Ranks once decided in the process of implementing a change by classification may change over the time until accomplishment of the change, making a reminder necessary that class will vary at the time of re-assessment done at implementation stages where appropriate, or at the time of review of the results obtained at change implementation.

The following are classification examples:

（1）"Change where impacts on quality become apparent" means a change that is likely

to have a significant impact on product quality and to become apparent in its impact, i.e. there is a risk of exerting an impact on design quality of the said product, and therefore, special attention should be given to safety and efficacy.

For example, the change in basic principles and methods of manufacturing procedures and quality control procedures corresponds to this case. Furthermore, changes in settings of parameters such as properties of raw materials, performance qualifications of equipment, and operational conditions etc., if they are assumed not to have been evaluated adequately in the past, in as far as past knowledge has been used, also correspond to this case.

In these evaluations, it is assumed that a change in quality characteristics may become apparent, making it necessary to evaluate/study sufficiently in advance, and also to implement evaluation and validation based on the rationale of suitability of specifications, etc. during the implementation process of the change. In addition, if there is a combination of multiple changes of conditions in equipment/processes, special attention should be paid to the validity of advanced prediction. Furthermore, if there is a selection from multiple technical elements, additional application of a Risk Assessment may become necessary as a means of implementation.

This change is considered to possibly conflict directly with or to potentially interfere with approved matters. Therefore, it may be required to request confirmation by marketing approval holders in advance and, additionally, to take requisite legal procedures for the "application for partial change in manufacturing approval", etc.

（２）"Change which impacts quality may potentially become apparent" means a change of which the impact on product quality cannot be denied. One example corresponding to this would be a change in which a change in the properties of product quality occurs, but stability within the scope of actual measurement results obtained in the past is expected when applying the data used for establishment of settings in parameters, such as properties of raw materials, performance qualification of equipment, and operational conditions etc, is considered. On the other hand, if it is a change for which the degree of changes is not clear or the impact is not predictable, a Risk Assessment must be done with special care during the evaluation of the change plan. It needs to be kept in mind that during the time course of implementation of a change, additional Risk Assessment may become necessary, and as a result, the class may shift to either "Change where impacts on quality become apparent" or "Change where there is no impact on quality".

（３）"Change where there is no impact on quality" means a change from which impacts on product quality is considered to be minimal. One example corresponding to this would be a change in which, in association with the change, a change in properties of product quality is assumed to be slight or no change occurs, in consideration of the data used for establishment of settings for parameters such as properties of raw materials, performance qualifications of equipment, and operational conditions etc. Normally, this change can be implemented within daily control based on the GMP, with the prerequisite

condition that the plant has appropriate procedures. Some renewal etc. of the operational equipment and instruments, written operational procedures, changes of written procedures for common unit operations in manufacturing, which are specified in the GMP, may fall under this category. If it is a facility etc. where facilities and equipment are shared with and used for the manufacture of multiple types of products, it is necessary to evaluate the impact of the change on each individual product manufactured. If it is a change that requires a re-validation of equipment especially , the classification will also change because of increased risk.

In this manner, the classification based on Risk Assessment is useful as a communication tool for sharing recognition, within a GMP organization and interrelationships with marketing approval holders, about the necessity of additional assessments and the rigidity of evaluation related to risk occurrence during change implementation. It is desirable to judge the acceptance of the risk of a change utilizing the results of assessment appropriately according to the magnitude of risk, and only after fixing the control content used during the implementation process, to implement the change.

6．3 Consequence Analysis of Impact of Change on Quality(Verification)

As to the results of implementation of a change, it is necessary to verify that there is no serious influence on targeted use or the method of use of products, and it must be confirmed that quality is unaffected in terms of product release. For this objective, evaluation must be done to verify that the quality of the product after the change is within the scope of quality that is suited for the targeted use, and that the objective of the change was accomplished as planned. At this evaluation, the impact on quality before versus after the change should be evaluated following a protocol specified in the analysis and testing methods and validation plan, etc. Additionally, it is important to confirm the validity of Risk Assessments done in advance. In the above Consequence Analysis, it is required to at least verify the following specification compliance, and according to the content of the change and characteristics of the products, additional tests should be considered. It is necessary to evaluate the quality before versus after the change, with recognition that the possibility of an impact on quality not detectable by the current specifications and testing methods cannot be denied.

（1）Confirmation of Specification Compliance

At evaluation of the impact on quality by the change related to said product, it is necessary to confirm that the qualities of intermediates of drug substances, drug substances, intermediate products and/or drug formulations, which are affected by the change, meet the predetermined specifications.

Herein, specification means not only approved specifications but also includes

self-specifications and standards such as in-process tests, etc, and it should be tested and analyzed with approved specifications and testing methods and with standardized process analysis methods. Furthermore, occasionally, modification of specifications and testing methods may become necessary at the time that a change is implemented.

Product quality after the change is evaluated from the aspects of specification compliance, and a variation before versus after the change, in specification items that are targets of trend analysis. Those in main characteristic values, that are in-process controlled, are also comparatively evaluated.

In evaluating the effectiveness of a change, product tests should be conducted not just for a single batch or a single lot, and trend analysis in quality, which is one of the effective tools in GMP control, should also applied.

（２）Additional Tests

At evaluation of the impact of a change on design quality, it is necessary to consider implementing evaluations of properties related to design quality of the product such as safety, efficacy and stability etc. which include chemical, physical, microbiological, biological properties, bioavailability, stability profiles etc. As evaluation at the time of change, it is necessary to not limit testing to that of products after the change, but to also to study whether or not it is necessary to implement additional tests including tests for intermediates, intermediate products, raw materials, reagents, materials for manufacturing, containers/plugging systems, etc. In addition, it is necessary to confirm that results of in-process tests show a similar trend before versus after the change.

Requisite additional tests vary depending on the content of the change in manufacturing, drug substances, characteristics of drug products, and the influence of the said product on quality. For example:

- At evaluation of changes in the impurity profile or degradation product profiles, profiling is done first using appropriate chromatographic techniques and then new impurities and degradation products are evaluated based on the observed changes in impurity profiles. In order to evaluate higher levels of impurities in products than before the change, toxicity studies may be implemented based on: "Guidelines for Impurities in New Drug Substances" , Ministerial Notification No.877 of September 25, 1995 by ELD, PAB, MLHW (Q3A); "Guidelines for Impurities in New Drug Substances (Revised)", Ministerial Notification No.1216001 of December 16, 2002 by ELD, PFSB, MLHW(Q3AR); "Guidelines for Impurities in New Drug Products (Revised) ", Ministerial Notification No.1204001 of December 4, 2006 by ELD, PFSB, MLHW(Q3AR2); "Guidelines for Impurities in New Drug Products", Ministerial Notification No.539 of June 23, 1997 by ELD, PAB, MLHW (Q3B); "Guidelines for Impurities in New Drug Products (Revised)",Ministerial Notification No.0624001 of June 24, 2003 by ELD, PAB, MLHW (Q3BR) ; "Guidelines for Impurities in New Drug Products (Revised) ", Ministerial

Notification No.0703004 of July 3, 2006 by ELD, PFSB, MLHW (Q3BR2).

- At evaluation of the impact on bioequivalence of the change in dissolution profile of solid dosage forms, it is necessary, for example, to perform dissolution tests that use several solutions of different pH, using several sampling time points other than the points specified in the specifications and testing methods. Furthermore, if necessary, *in vivo* bioequivalence tests should also be considered.

It is important to cautiously judge whether or not there a significant change in the repeatability of specification compliance and in design quality, using a multi-faceted evaluation, if necessary, for main characteristics of the product. In order to confirm quality consistency, it is necessary to consider making a plan for selecting additional test items to be confirmed by periodic review, deciding the requisite number of consecutive lots to be evaluated starting immediately after the initiation of change implementation, or making a plan to skip tests, according to the magnitude of the risk of a change.

7. Procedures for Change Control in GMP

For a Change Control in GMP, it is required to confirm, by implementing the assessment of the impact of change on product quality, that quality is maintained as an important property throughout, before versus after the change. In addition, for this object, it is required that a control system in which approval by the quality unit is an essential element, and procedures for the control be established.

The following are procedures for Change Control of GMP, and points to be given attention. These items are also shown in chapter 12 "Change Control" of "GMP Guidelines for Drugs/Quasi-drugs (Products)".

12.10 Changes attributable to stipulations in laws, etc, in addition to changes attributable to complaints and recalls etc should be subjected to Change Control.

12.11 As changes involving "the documents related to change control procedures prepared pursuant to stipulation in Article 8, Paragraph 4 of GMP Ordinance for Drugs/Quasi-drugs" (hereinafter referred to as "Change Control Procedures"), changes related to the system for management/control of quality, raw materials and materials (including changes in suppliers), specifications, manufacturing methods, analysis and testing methods, and building and facilities (including relevant software) should be included.

12.12 Change should be drafted and reviewed by the appropriate unit or units, and approved by the quality unit.

12.13 Change Control Procedures should include the following:

1) Evaluation of the necessity of re-validation, the necessity of additional test analysis and testing required for the validity of a change, and the necessity of application for partial change in manufacturing approval, as one of the evaluations in Article 14, item 1 of GMP Ordinance for Drugs/Quasi-drugs,
2) To establish evaluation methods for product quality after the change (including accelerated stability tests and stability monitoring measurement programs etc) and acceptance criteria, prior to the change.
3) To establish procedures for the revision of documents related to a change and for the training of personnel, prior to the change, to definitively implement the revisions of the document and the training.
4) To decide whether or not it is necessary to revise specifications and testing methods, shelf-life/expiration-date, and labeling, prior to the change, as one of the other necessary measures in Article 14, item 2 of GMP Ordinance for Drugs/Quasi-drugs,

12.14 To initially evaluate several lots of the product manufactured and to analyze them in the changed state after the implementation of a change.

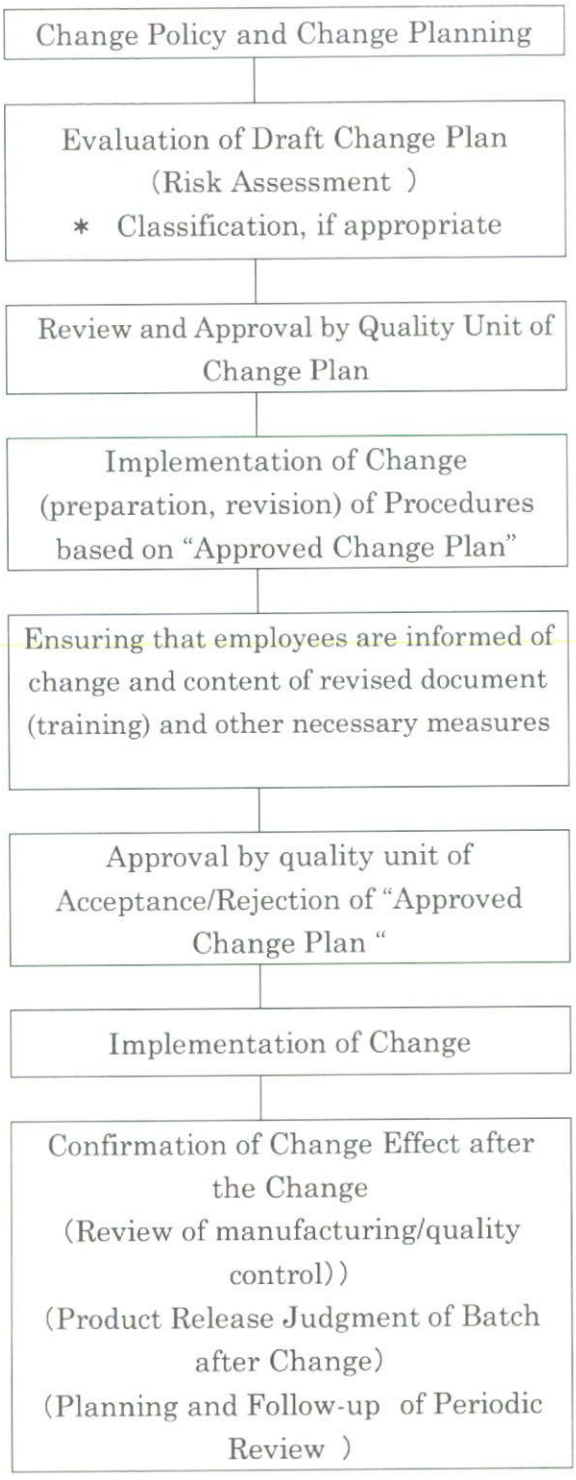
Procedures of Change Control should be defined and documented under the GMP organization and system of manufacturers. Procedures should be defined according to each organization, and the primary items in procedures of Change Control are that 1) the validity of each change should be approved by the quality unit and 2) documented.

The quality unit should be given the authority to approve Change Control, and Change Control manager and persons in charge of Change Control should be assigned in advance.

An appropriate unit in the organization prepares a draft of a change, and the draft is evaluated for its necessity, validity, impacts on product quality, etc. The change after this evaluation is prepared for implementation only after approval by the quality unit. Revision/alteration of procedures, etc. should be done appropriately, followed by training of personnel and other necessary measures should be taken, and then, operation after the change should be implemented. A series of these measures should be documented, and preserved. An example of basic procedures is shown below.

Meanwhile, it is allowed, in consideration of inclusion of multi-faceted viewpoints as a form of Risk Management, to operate Change Control in a organization such as a "Change Control administrative office" or a "Change Control committee" consisting of a manager and several of staff members in charge.

Example of Change Control Procedures in GMP



8．General Requirements in Control of Documents related to Change

At implementation of a change, it is essential that the documents pertaining to said change are revised in accordance with predetermined procedures for change, and approved by the authorized person, because documented items usually become a target of the change.

All contents of a change should be documented and controlled. As to a document for Risk Assessment, it is useful to show the validity of a change, thus making it is desirable to preserve it in files related to procedures for Change Control.

It is desirable to establish procedures in which all results of Change Control implemented based on the GMP are listed together with results of handling applications for partial change in manufacturing approval etc., and printed in annual reports. This is an effective method of showing how appropriately Change Control procedures are carried out.

9. Collaboration of Manufacturers and Marketing Approval Holders

The one who implements a change is the manufacturer, but an appropriate collaboration between manufacturers and marketing approval holders is indispensable for maintaining the consistent quality of drug products. This chapter deals with the collaboration between manufacturers and marketing approval holders which becomes necessary at the time of a change.

9. 1 Handling of Change Control

As a result of revision of the Pharmaceutical Affairs Law of 2005, Change Control is now a requirement of the GMP. In "Ministerial Ordinance on Standards for Quality Control for Drugs, Quasi-Drugs, Cosmetics and Medical Devices" (GQP Ordinance), the marketing approval holder is required to supervise manufacturers and Change Control of manufacturing is defined as one of the items to be supervised (in Article 7, item 5, and Article 10, Paragraph 3; and therefore the marketing approval holder and the manufacturers should address Change Control jointly and appropriately).

9. 2 Change Communication

It is likely that technology information (research and development information, etc.) disclosed by the marketing approval holder to the manufacture is limited Therefore, it is very dangerous for the manufacturer to make a judgment alone about acceptance or rejection of a change .It is a principle that the manufacturer notifies the marketing approval holder about any change, if it has a possible impact on quality, regardless of the size of that probability. However, the targets subjected to Change Control, which are handled by the manufacturer, are vast, ranging from "something directly related" to manufacturing/marketing products to "something absolutely not related", such that it may be not rational that the marketing approval holder decides acceptance or rejection

for every item after judging impacts on product quality for every change in manufacturing plants. For this reason, the marketing approval holder needs to explain sufficiently to the manufacturer the idea of what changes notification should be given for. Providing the manufacturer with tools such as the classification of Change Control communication and communication methods, together with examples thereof, is useful for Change Control communication.

9．3 Collaboration about Information

Generally speaking, the situation is that the marketing approval holder has the technological information on research and development of a drug product, but does not sufficiently grasp the technological information obtained in actual manufacturing fields. The manufacturer, on the other hand, can obtain only limited information on research and development, but can accumulate the technical information obtained in actual manufacturing fields. In consideration of these circumstances, the marketing approval holder should provide information on research and development thereby supporting the manufacturer in the planning of a change such that the manufacturer can implement the evaluation appropriately without omitting the impact of the change on product quality, according to necessity. Furthermore, the manufacturer should provide various forms of appropriate technical information and experience related to the actual production, as the one well informed about manufacturing sites (actual production).

In order to appropriately carry out "6.2 Risk Assessment and Classification of Change" and "6.3 Consequence Analysis of Impact of Change on Quality (Verification)", both the marketing approval holder and the manufacturer should clearly realize that appropriate mutual disclosure of information to each other and collaboration between the two parties are indispensable.

9．4 Collaboration with Other Manufacturers

In cases where multiple manufacturers are involved in the manufacture of a drug product, there is a possibility that a change in a process by one manufacturer will exert an influence on a processes etc. of the manufacturer of the next step (hereinafter referred to as "the next step manufacturer"). Therefore, the marketing approval holder should provide information on the content and timing etc. of a change not only to the manufacturer who executes the change but also to the next step manufacturers in advance. Naturally, if a change is one which requires quality evaluation or equipment investment, collaboration with the next step manufacturers should be initiated appropriately from the planning stage.

On-site Visit
OPS / OC / ONDQA / OGD

Yukio Hiyama, Ph.D.
Chief, Third Section, Division of Drugs
National Institute of Health Sciences
1-18-1 Kamiyohga, Setagayaku, Tokyo 158-8501

October 1 and 2, 2007

Day 1

8:00	OPS Meet and Greet	Helen Winkle Jon Clark Ted Sherwood
8:30	Transit to Office of Compliance	David Morley
9:00	Introductions and Manager Discussions	Deb Autor Joe Famulare Rick Friedman
9:30	Pre-approval Inspection	Alicia Mozzachio Doug Campbell
10:15	Break	
10:30	CGMP Conformance / Surveillance Inspection	Alicia Mozzachio Doug Campbell
11:00	Inspection Site Selection Model: Design and Operation	Gregg Claycamp PhD
11:30	Closing Remarks and Discussion	Deb Autor Joe Famulare Rick Friedman
12:00	Lunch with OC	
12:45	Transit to OGD	Rick Friedman
1:00	Generic Drug Application Review Process and Practices – Role of USP standards in review – OGD Question Based Review	Gary Buehler
2:30	Break	

2:45	Discussion / Q&A	
4:00	Adjourn	
4:30	Dinner (with Moheb and other FDA managers)	

Day 2

8:30	ONDQA Overview – NDA Review Process – CMC Pilot	Moheb Nasr / Chi-wan Chen
10:00	Seminar (Research or Regulatory Topic) Conference Room 2205	Yukio Hiyama
11:00	Q & A	
11:30	Lunch	Moheb, Chi-wan, Arzu, DDs
1:00	Division of Pre-marketing Assessment I	Blair Fraser Ramesh Sood Ali Al-Hakim
2:00	Division of Pre-marketing Assessment II	Elaine Morefield Moo-Jhong Rhee Norm Schmuff
3:00	Break	
3:15	Division of Pre-marketing Assessment III and Manufacturing Science	Rik Lostritto Ravi Harapanhalli Christine Moore
4:15	Division of Post-marketing Evaluation	Eric Duffy Jim Vidra Hasmukh Patel
5:15	Wrap-up	Moheb Nasr / Chi-wan Chen

An Overview of the Office of Generic Drugs

Timothy Ames, R.Ph., M.P.H.
Chief, Review Support Branch
Office of Generic Drugs
October 1, 2007

Office of Generic Drugs Mission Statement

To ensure through a scientific and regulatory process, that generic drugs are safe and effective for the American public.

2

Did you know that generic drugs...

- Are safe and effective alternatives to brand name prescriptions
- Can help both consumers and the government reduce the cost of prescription drugs
- Generics represent 63% of the total prescriptions dispensed in the US, but only 20% of all dollars spent on prescription drugs. *
- Save approximately $53 for every prescription sold.

*Source: Generic Pharmaceutical Association, *GPhA Praises House Subcommittee for Increasing Funding for Office of Generic Drugsbout Generic Pharmaceuticals*, 7/25/07. http://www.gphaonline.org

Breakdown of FTEs – Office of Generic Drugs

Total	214
♦ Chemists	84
♦ Bioequivalence/Pharmacologists	32
♦ Pharmacist/Project Managers	66
♦ Medical Officers	3
♦ Math Statisticians	3*
♦ Microbiologists	8
♦ IT Specialists	2
♦ Admin/Support Staff	19

*(do not belong to OGD)

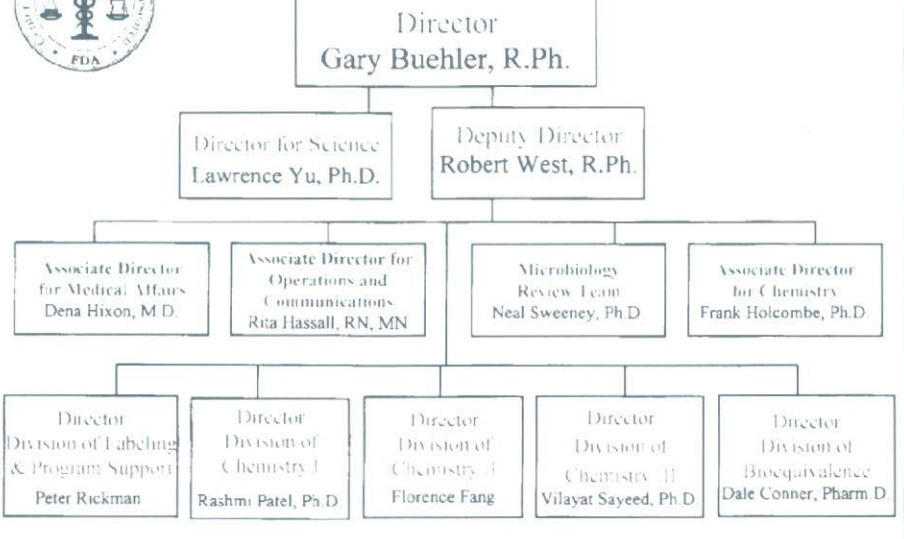
4

OGD Major Responsibilities

- Review and Approve Abbreviated New Drug Applications(ANDAs)/Supplements
- Provide Regulatory/Technical Guidance to Industry (Controlled Documents)
- Address Scientific Issues concerning Generic Drug Products (Citizens' Petitions, etc.)
- Develop/Improve Review Processes for ANDAs
- Educate & Train a diverse staff in latest Scientific, Regulatory, and Review technologies
- Educate American Public about FDA approved Generic Drug Products

5

Office of Generic Drugs



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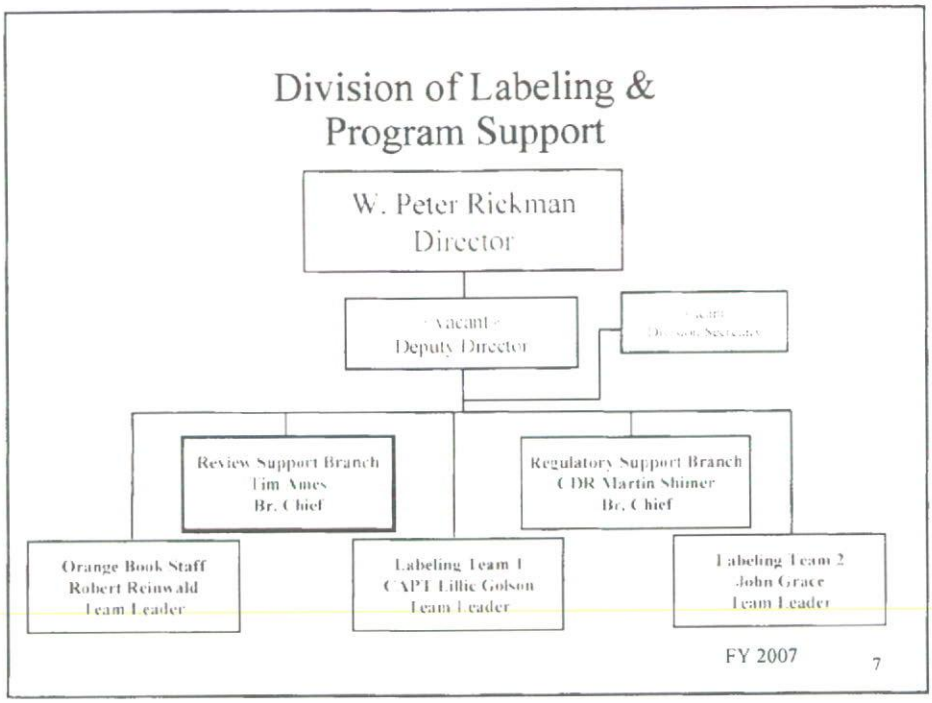
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Program Support
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Director
Deputy Director
Review Support Branch
Tim Ames
Br. Chief
Regulatory Support Branch
CDR Martin Shiner
Br. Chief
Orange Book Staff
Robert Reinwald
Team Leader
Labeling Team 1
CAPT Lillie Golson
Team Leader
Labeling Team 2
John Grace
Team Leader
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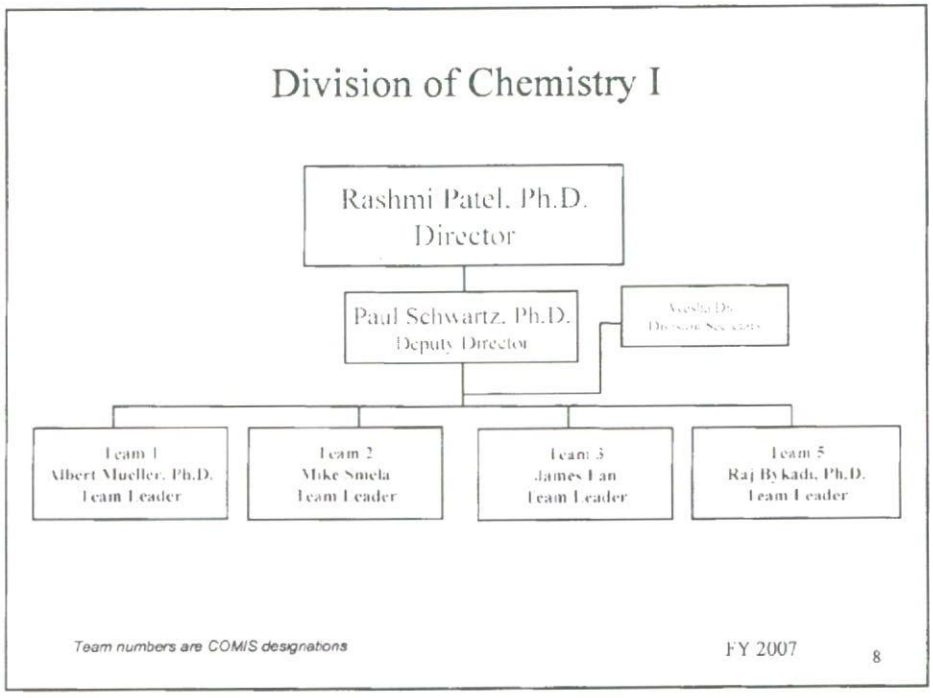
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Paul Schwartz, Ph.D.
Deputy Director
Team 1
Albert Mueller, Ph.D.
Team Leader
Team 2
Mike Smela
Team Leader
Team 3
James Lan
Team Leader
Team 5
Raj Bykadi, Ph.D.
Team Leader
Team numbers are COMIS designations
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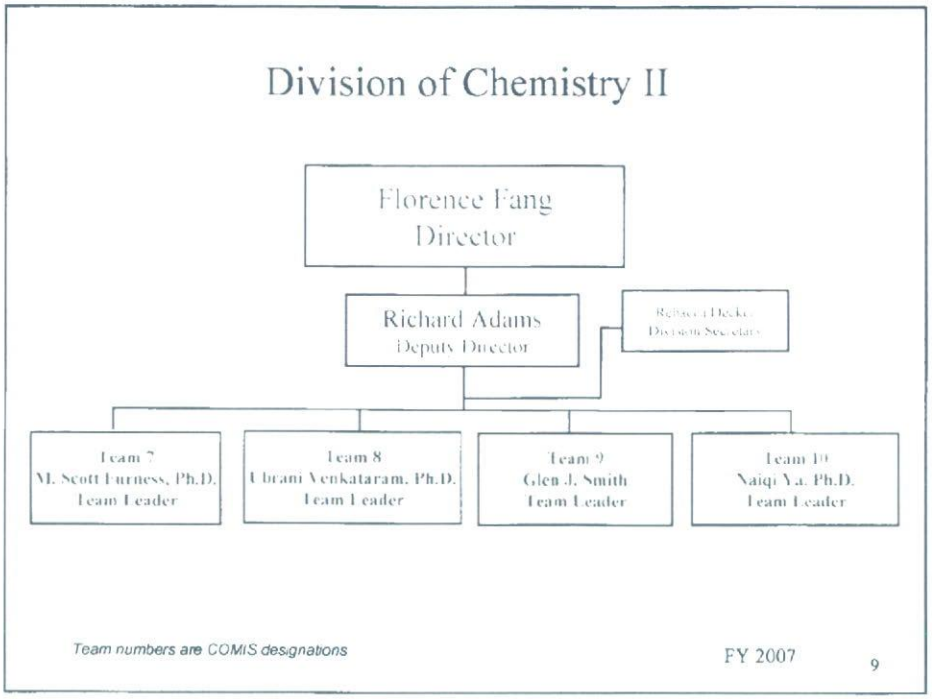
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Richard Adams
Deputy Director
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M. Scott Furness, Ph.D.
Team Leader
Team 8
Ubrani Venkataram, Ph.D.
Team Leader
Team 9
Glen J. Smith
Team Leader
Team 10
Naiqi Y.u. Ph.D.
Team Leader
Team numbers are COMIS designations
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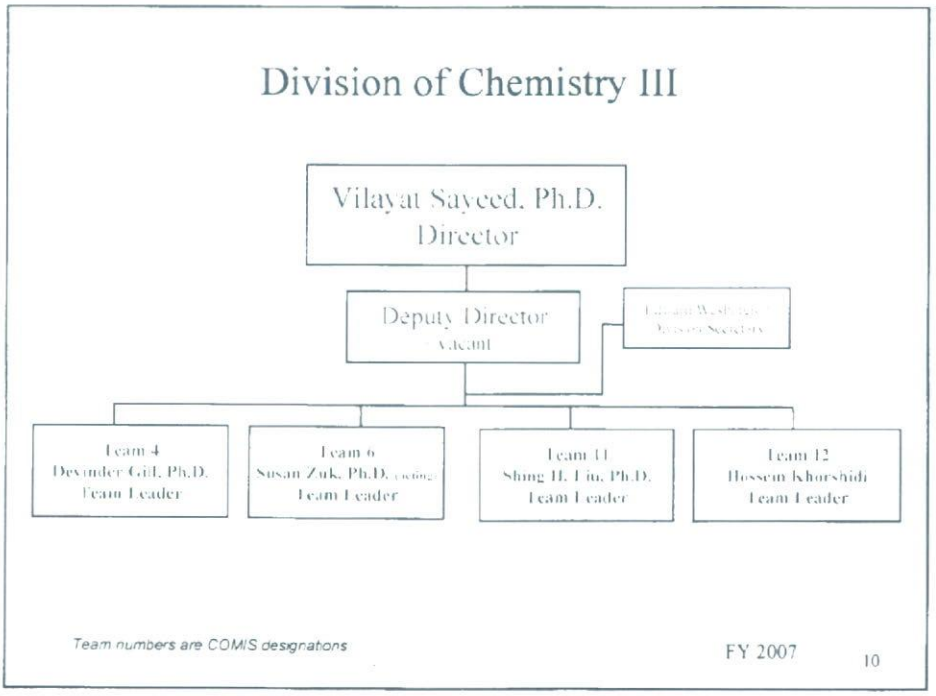
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Deputy Director
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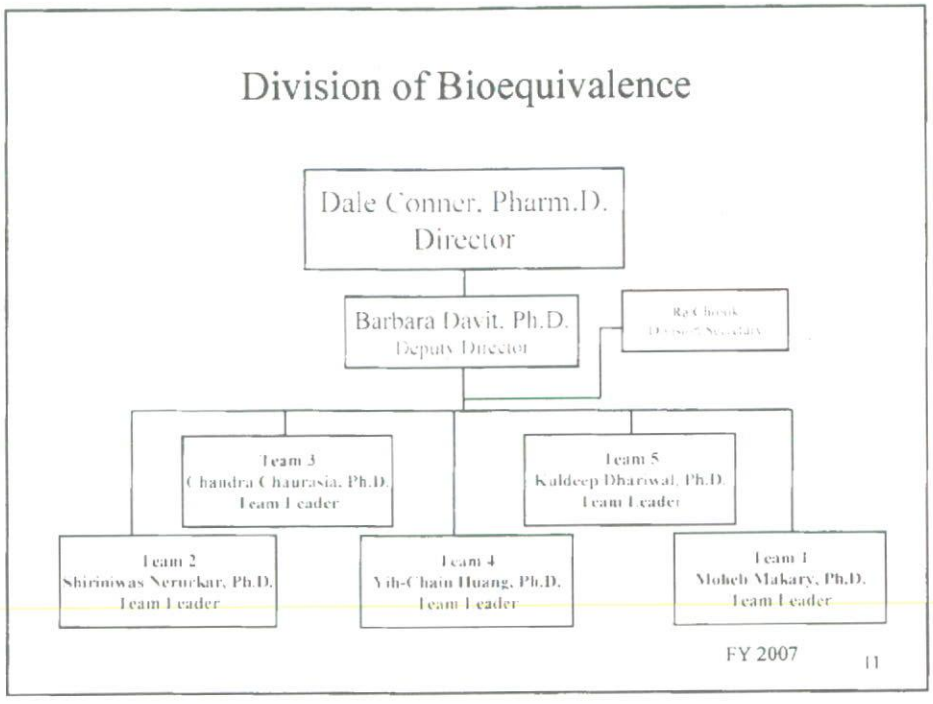
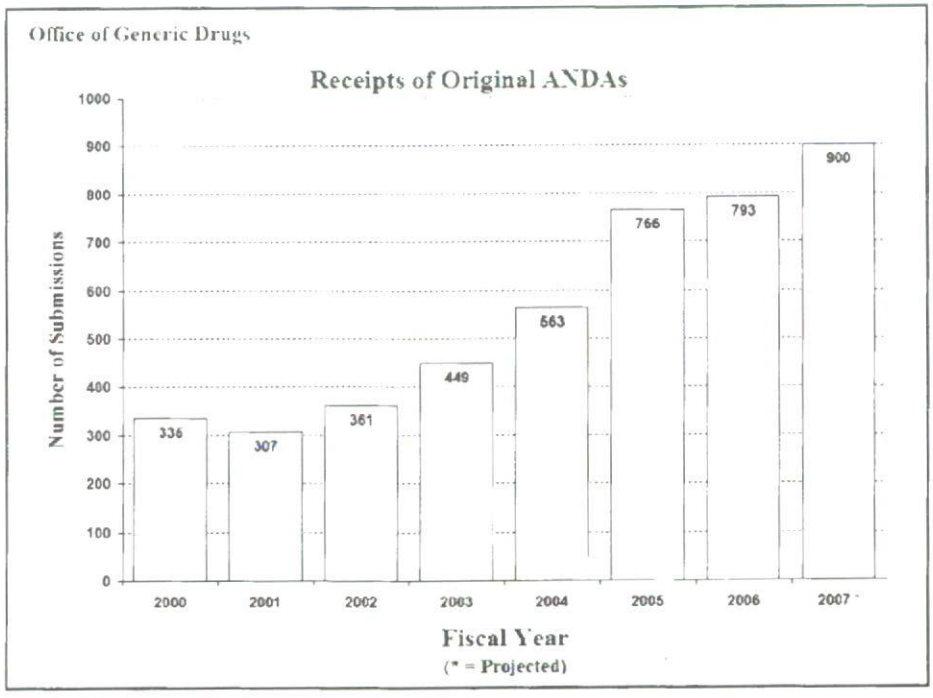
Team 4
Devinder Gill, Ph.D.
Team Leader
Team 6
Susan Zuk, Ph.D.
Team Leader
Team 11
Shing H. Liu, Ph.D.
Team Leader
Team 12
Hossein Khorshidi
Team Leader
Team numbers are COMIS designations
FY 2007
10


Division of Bioequivalence
Dale Conner, Pharm.D.
Director
Barbara Davit, Ph.D.
Deputy Director
Team 3
Chandra Chaurasia, Ph.D.
Team Leader
Team 5
Kuldeep Dhariwal, Ph.D.
Team Leader
Team 2
Shiriniwas Nerurkar, Ph.D.
Team Leader
Team 4
Yih-Chain Huang, Ph.D.
Team Leader
Team 1
Moheb Makary, Ph.D.
Team Leader
FY 2007
11


Office of Generic Drugs
Receipts of Original ANDAs
Number of Submissions
1000
900
800
700
600
500
400
300
200
100
0
336
307
361
449
563
766
793
900
2000
2001
2002
2003
2004
2005
2006
2007
Fiscal Year
(* = Projected)