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ISO-GUM and Supplements are Utilized for QA of BCA Data

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1. Introduction

International Organization of Standard- Guide to the expression of Uncertainty in Measurement (ISO-GUM)[1] was published as guidance for making a measurement result into an assurance performance by ISO in 1993 and in 1995 corrected. ISO has inquired by adding new thinking to the conventional method. To apply the GUM approached two main assumptions must hold. One is used expression of uncertainty from error so that it might be suitable for an assurance in evaluation of ambiguity measurement data. Another one used Exploratory Data Analysis (EDA) for ambiguity data from classical statistical analysis. It is now useful in order that the Blood Chemical Analysis (BCA) may also grade up the reliability of an analysis result with assurance performed.

ISO was additional new issue that is published many supplements in order to fully utilize ISO-GUM. Particularly, it is come to be for Markov Chain Monte Carlo (MCMC) in Bayesian inference and. the come to be used Multi-viable Analysis (MA) that is useful the multi regression analysis by multi-nonlinear least squares method. One of them is a production procedure for obtaining an assurance process. ISO-GUM is respectively as one by one step, it is progressing [2]. The result is also required by improvement of in measurement accuracy and Quality Assurance (QA).

2. Background of ISO-GUM

In planning measurement system is very important for Measurement Systems Analysis (MSA) [3]. It is a specially designed experiment that seeks to identify the uncertainty components in the measurand. MSA is used to evaluate the quantitative analysis in medical test system which is entire process of obtaining data. The inspector has to understand well the process of measurement system used in order to ensure the obtained Data Quality Object (DQO) and has strived for quality analysis in good assessment. Many mistakes in the total testing process are called “laboratory errors” [4], although these may be due to poor communication or poorly designed, all of which are beyond the laboratory error control. The uncertainty element in total measurement system is recognized to be an error of measurement management poor. At the management all the processes need to be managed from the preceding paragraph of laboratory analysis to the processing an after and an end. It has to remove the fault element and risk element of clinical healthcare by the uncertainty

data. In order to improve supply service of data from laboratory, it require to QA of the data offered.

The role of global and regional metrological organizations is also to be discussed to get a mutual confidence between these test laboratories. The main targets of above activities may be summarized by the Mutual Recognition Agreement (MRA) between participating economies.

ISO-GUM published for an international consensus based on this concept, it is emerging that analysis values are expressed in combination with uncertainty of their measurement to indicate their reliability. In the field of measurement science and clinical chemical analysis, there is exists world wide requirements for the reliable and competitive evidence to confirm the measurement process and measurement results in many stages. A goal of object is improvement in the reliability as Good Laboratory Practice (GLP)

The purpose is in construction of MSA for without hesitating diagnosis since some inspect data is ambiguous. It is selecting a point of healthcare for always suitable diagnosis, and losing the futility of a health resource. For this reason, it aimed at starting with improvement in the accuracy in the field of BCA as a trial to MSA and assuring the quality of result completely by a laboratory implement guide. The goal of good practice guidance research has continued in the post to support the development of Quality Assurance (QA) and Quality Control (QC) in Quality Engineering (QE) completely by high order accuracy. ISO-GUM was legislated an accuracy assurance for dealing of measurement data.[5]. It is ISO15193:2009 that is defined as in vitro diagnostic medical devices.

ISO/IEC Guide 98-1:2009 provides a brief introduction to be GUM in order to indicate the relevance of that new fundamental guide and promote its use. It also outlines documents related to the GUM that are intended to extend the application of that guide to broader categories and fields of practical problems. It also considers various concepts used in measurement science [6] that is included a science (thinking) and an engineering (thinking). In particular, it covers the need to characterize the quality of a measurement though appropriate statements of measurement uncertainty. ISO edited international vocabulary in metrology (VIM) simultaneously.

2.1 QA and QC

Measurement data condition are roughly divided into within-laboratory and between-laboratory for QC. Under within-laboratory measuring condition, the uncertainty due to within-day variations are estimated from repeatedly measured values of the test sample within the same laboratory. As for research target in clinical examination, the accuracy of Internal Quality Control (IQC) in house must be keep always more than two sigma. The under between-laboratory measuring condition, the uncertainty due to compared between another laboratory variation data. The uncertainty due to between-laboratory variation are estimated from simultaneously measured values of the test sample obtained at more than one laboratory, and an accuracy of External Quality Control (EQC) secures more than three sigma levels, it is an international level. In both case, the individual component are composed to obtain standard uncertainty due to measurement conditions. The lack of certainty, a state of having limited knowledge where it is impossible to exactly describe

existing state or future outcome, more than one possible outcome. Necessity of more than the three sigma accuracy was carried out to IT medical system for world wide base medical healthcare. Especially an External Quality Assurance Scheme (EQAS) is an importance it can use also for common view of medical cognitive diagnosis technology. If the final report value of BCA became a commercial transaction article, it requires to follow the QA by ISO standard. Quality Engineer (QE) is a means also to prevent a misdiagnosis effectively. Furthermore, the Statistical Quality Control (SQC) of a patient individual's data is also important for prevent from a clinical misdiagnosis. The result of a statistical analysis is working not only get to know condition of disease, but it is utilized for exacted judge decisions to support a point of care program. The accomplishing to this requirement, some international regulations and guides has been edited as the results of joint works among several international organizations for data quality.[7][8]

QA is doing its best also in the field of a clinical examination to be able to respond to a patient or a donor effectively. ISO-GUM is edited in series to 98-1 from 98-5 as a guide of ISO/IEC. QA of clinical test by ISO-GUM is made utilization in 2006.

2.2 ISO and QE

2.2.1 Measurement error

The conventional statistical technology was researching for error of random data by the subjective statistical work by "law of large number", it is come out complicated random error and systematic error. Systematic error can be removed as bias since it can be made a fixed numerical value. Random error was difficult work in order to remove. Therefore, the result in which reading out and clear not able to achieved. Further, the first type error (false positive) and the second type error (false negative) are achieved among the errors. So it had become a cause of the misdiagnosis. For prevent a misdiagnosis, it is required to correct all of the errors factor. Work of an improvement of these errors has been also studied by fault state through many years in the Quality Engineering (QE). The central pole theorem became important recently. Many technologies were useful commonly in QE and in ISO-GUM [8].

2.2.2 QE

QE assumes how often a fault state generative, it is starting analysis from hierarchical gradient-based motion estimation of fault factors though "Failure Mode and Effects Analysis (FMEA)". QE determines the root cause of the fault element though "Root Cause Analysis (RCA)" and "Fault Tree Analysis (FTA)". These are developed based on tracer technology. In professional Test (PT), the procedure of decision followed one by one, in order to discern the importance level of fault factors.

FTA is versatile methods for dealing with probabilistic risk, reliability and availability. Although FTA was developed in the 1690s for hardware system, it is an adaptable logic-based technique that has been applied to combined hardware and software systems. This research was led it to make the result of the BCA The relation between QE and ISO-GUM is shown in table 1.

Term	ISO-GUM	QE
process	key comparison. and law of propagation of uncertainty.	FMEA. FRACAS FTA and RCA
Estimation	uncertainty.	Random error
Algorithm	MCMC model Multi-variable analysis.	Quadratic equation.
expression	illustration.	formula
result	confidence interval	tolerance
critical	reference	standard
unit	SD	%
system	legislation	Scientific thinking Technical thinking
Focus	normal and abnormal distribution	normal distribution
test	effective free degree	parametric nonparametric
Estimation	Uncertainty.	error
Algorithm	MCMC modeling. Multi-variable analysis.	Quadratic equation.
expression	illustration.	formula
result	confidence interval	tolerance
critical	reference	standard
Focus	normal distribution and abnormal distribution	normal distribution only
test	Nonparametric & nonlinear	Parametric & linear

Table 1. Comparison ISO-GUM and QE

2.2.3 DL/AMD

Present are procedures based on modern Bayesian statistics which are used calculate characteristic limit i.e. the decision threshold, detection limit and confidence limit in BCA. Indicated are also key elements of this statistics which can be used for measurement of Decision Level/Amount Minimum Detectable (DL/AMD), DL applied to the activity result. AMD was the detection criterion that was insensitive to sample specific variables such as chemical yield and detector efficiency. The example of instrumental enzyme activation analysis provides an illustration of the issues discussed.

DL/AMD was able to profit by the operation. QE has developed for the QC of industry as 6 sigma level. However, these have been processed by the regression analysis by making subjective frequency probability of a statistic value into normalized distribution. Regression analysis is applied the least squares method. An occurrence probability of the statistics value of a fault element which is accompanied element by a natural variance, it becomes an abnormal distribution in many cases.

In the result of research, “Decided level/Minimum Detectable Concentration (DL/MDC)” are other different taxonomy of uncertainties and decisions that include a more broad sense of uncertainty and how it should be approached from an ethics perspective. Vagueness and ambiguity are some times described as “second order uncertainty”, there is uncertainty even

about the definitions of uncertain states or outcomes. The difference result is that this uncertainty is about human definitions and concepts not an objective fact of nature. It has been avoidable while uncertainty (first order).

2.2.4 Probability Density Function (PDF)

PDF expresses distribution of uncertainty (see Fig1). Assignment of a PDF to a quality analysis is using the Principle of Maximum Entropy (PME). There are existence two great traditions. One is probability theory what think is likely trueness of population mean, and second is confidence interval analysis what we know to be total error. Total error is system error plus random error. Probability bounds analysis gives the same answer as confidence interval analysis does when only range information is available. It being careful is that arises between total error and a confidence interval in many cases that example is abnormal distribution, which better as for evaluation uncertainty for QA. A normal distribution is comfortable in estimating the width of variation; it is fundamental statistical quantity by analysis of variance (ANOVA). If also gives the same answers as Monte Carlo analysis does when information is abundant. If it is an abnormal distribution, a setup will became difficult about a trueness value, and the reference value by ISO-GUM is then calculated for QA [10]

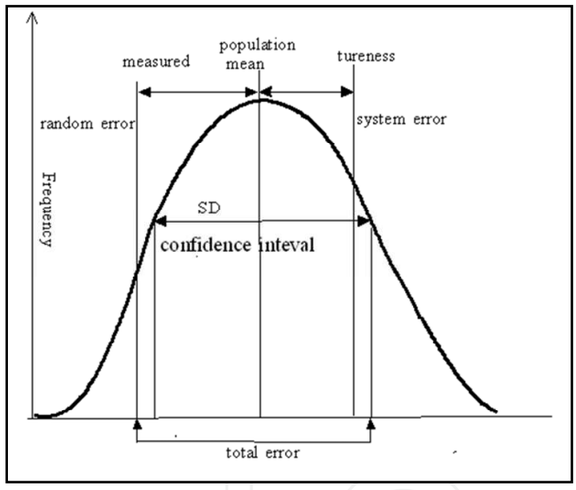

Fig. 1. Express of error and confidence interval

2.2.5 ANOVA

In measurement model, input quantities are measuring data of random variable that is interest as many components, $x=(x_1,x_2,\ldots,xi)$, then it can quote a functional relationship between measurement result Y and input quantities $f(x_i)$, as (1)

$$Y=f(x_1,x_2,\ldots,x_i). \quad (1)$$

Where, Y stands for the output quantity, that is the measurand in VIM, whereas x_i for multi input quantity. This is a model with one output which is adopted in the current ISO-GUM. A normal distribution is comfortable in estimating the width of variation of fundamental statistical quantity; namely, Root Sum Square (RSS), arithmetical average (mean), Standard Deviation (SD), Coefficient of Variance (CV) and etc. [18]

One of most import indicator of random error is time. In ANOVA, QA of measurement data must be considered error theory and effective ecologically so that basically, when null hypothesis is set up in kinetic state. It quotes a time series function. This rule is shown that the dependence is trueness function f(x,t) and it is include error factors g(x,t), as (2)

$$dx/dt=f(x,t)+g(x,t) \tag{2}$$

These are assumed as independent function. When an error factor exists by plurality, Burger's formula is adapted to Multi-variable analysis (MA) that has one or more g(x.t). ISO-GUM evaluates by reference value, even when a trueness value is unknown, and error serves as uncertainty.

Bayesian theorem grows from the simple principle that two random variables factor t and x remain in the following dependence: as (3). Vertical arrow | indicate conditional distribution.

$$P(xt)=P(x\,|\,t)*P(t)=P(t\,|\,x)*P(x) \tag{3}$$

$$P(x\,|\,t)= P(x\,|\,t)*P(x)/\ P(t)$$

2.2.6 Key comparison and reference value

If the trueness value was unknown, ISO-GUM is changed into reference value from trueness value, it is gating in the posterior data base that is set up by the EDA as frequency hypothesis and it does check with a Key Comparison (KC) method. KC is comparing between null hypothesis and frequency hypothesis.

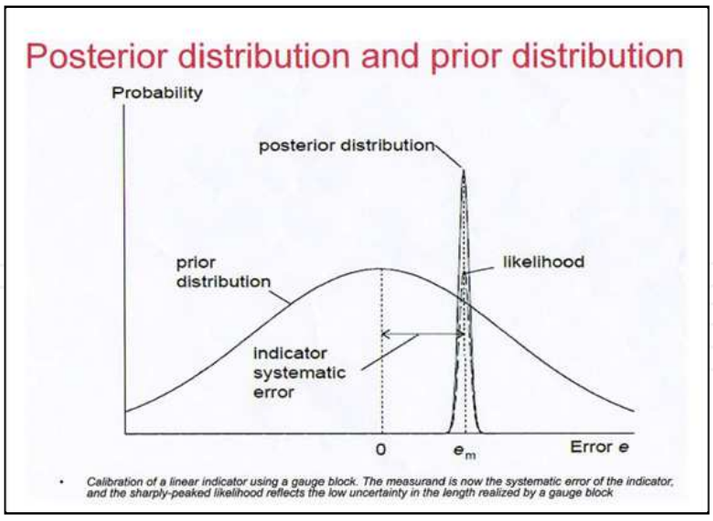

Fig. 2. Posterior distribution and prior distribution

Null hypothesis is making guesstimate uncertainty from prior distribution with an experiment data. Frequency hypothesis is made posterior distribution on data base that is standard posterior distribution. Reference value estimated with in likelihood position in Fig.2. [15]

2.2.7 EDA

Exploratory Data Analysis (EDA) in ISO-GUM calculates one by one until an assurance execution that is according to "Law of the Propagation of Uncertainty (LPU)". It is same as RCA and FTA [9] in QE. Work progresses aiming at goal of full implementation of an assurance. ANOVA is used "Law of the Propagation of Laboratory error (LPE)".

2.2.8 MCMC

Markov Chain Monte Carlo (MCMC)[4] determines numerically a PDF. A set of possible states or outcomes it where probabilities is assigned to abnormal distribution. This also includes the application of PDF to continuous variables.

MCMC is proposed for the calculation uncertainty which can be considered to the primary other method than statistical method to EDA in ISO-GUM. Result is illustrated to easy understand. MCMC follows from "Derivation" of Markov formula and the Monte Carlo method is based on the central limit theorem, it is include Gibbs sampling and Metropolis - Hastings (M-H) algorithm.

In probability and statistics, the t-distribution or Student's t-distribution is probability distribution that arises in the problem of estimating the mean of a normally distributed population when the sample size is small. It is the basis of the popular student's t-test for the statistical significance of the difference between two sample means, and for the difference between two population mean. The Student's t-distribution is a special case of the generalized hyperbolic distribution. Student's distribution arises when the population standard distribution is unknown and has to be estimated from the data. As it is in nearly all practical statistical work, problems treating the standard deviation as if it were known are of two kinds:

1. Those in which the sample size is so large that one may treat a data-based estimate of the variance as if it were certain.
2. Those that illustrate mathematical reasoning, in which the problem of estimating the SD is temporarily ignored, because that is not the point that the author or instructor is then explaining.

Example of MCMC is recommended in Fig 3 by NIST. There are making the three kind distributions from measured data of abnormal distribution. One is the rectangular (uniform) probability distribution, that are possible for setting six value of primary confidence interval easily and none is preferred against any other value, the probability for any value to be on top after throwing one dice is 1/6 that is derived by Markov formula. Second is t-distribution that is important in both theory and practice. And confidence intervals derived from Student's t-distribution with n-1 degree of freedom. The parameter is called the number of degree of freedom. It is the same as a 95% confidence interval. Third is normalized distribution that is converted from abnormal distribution by regress analysis. Three kinds distribution is analyzed in Fast Fourier Transform (FFT) series, and carry out is a combined Fourier synthesis that is making new confidence interval by ISO-14253-1 (see 3,5) in Gaussian distribution. In next step, Inverse Fast Fourier Transform (IFFT) is made the convolution of Gaussian distribution F(u) there, F(u) is made to the Cumulative Distribution Frequency (CDF) that is alternatively referred to in the literature as the

distribution function. CDF is compared in comparator, it be able to find out the fault point on the curve, and it is required to exploratory the cause of generating fault state further. U is carried out a final standard uncertainty Us that is affinity (Binding ratio P*Q/Po= %) in this case. Fig.3 has a spare input port for special form distribution e.g. triangular distribution, U form distribution. A result same as a fuzzy member function instead of FFT is useful.

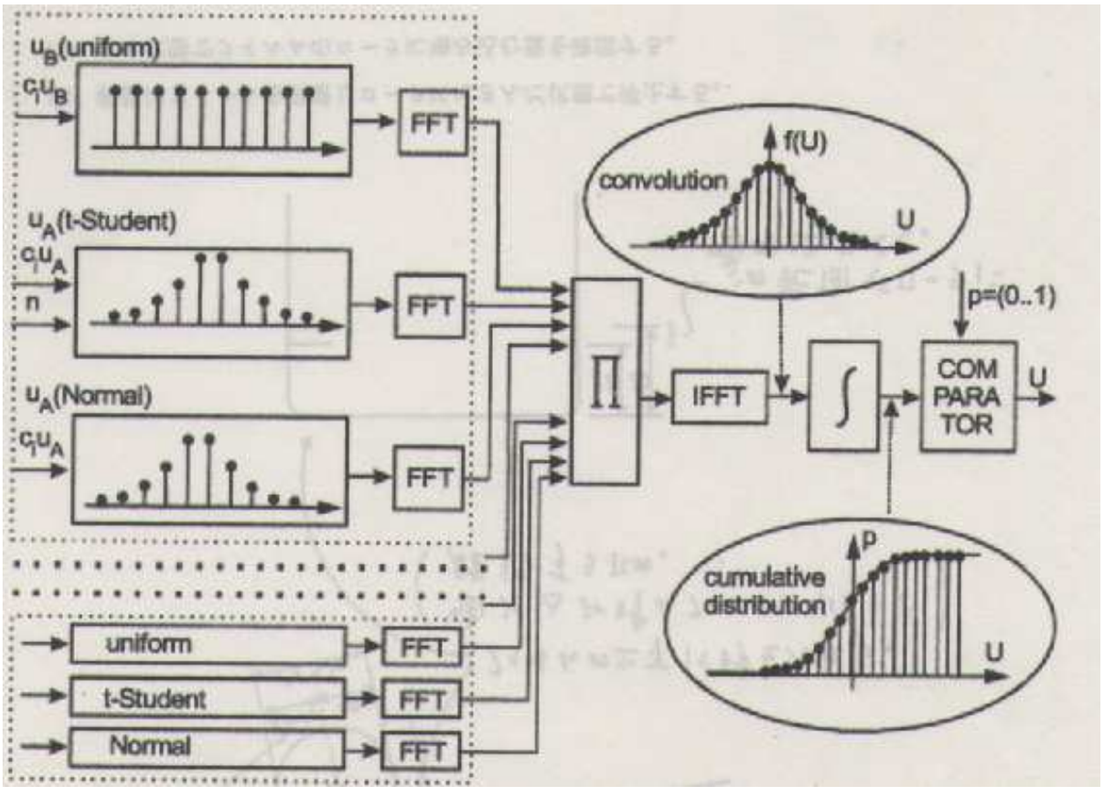

Fig. 3. MCMC of EDA in 2002 by rule of NIST

2.3 Uncertainty

2.3.1 Uncertainty theory

Uncertainty is defined "A parameter, associated with a result of a measurement, that characterizes the dispersion of the values that could reasonable be attributed to the measurand." in VIM.

The uncertainty data can usefully in 2 stage ways according to how they are estimated.

1. The first stage is utilizing the Bayesian inference of key comparison according to LPU.
2. The second stage analyzes is grouped into two categories the measurement result into type A and type B, according to determined the distribution condition. An importance distinction between both types of statistics lies in a quite different approach to the concept of probability.

The conventional concept of probability in statistics is associated with the relative frequency of random events. Such a statistics fails in case of systematic effect. Non-linear measurement

models, uncertainty values measured close to detection limits. Gibbs sampling is used for collection of data by double samples.

Uncertainty associated with measuring operations within the same laboratory is estimated by applying the nested analysis of multi-variance method though experimental data with between-day and within-day variation and sample vial as relevant factors. Specifically, a calibration line is generated at a time of every experiment during same days of experiment period. The thus obtained measured values examined for outliers. If outlier is found, its cause is identified and the rarely value is removed. If a problematic finding is obtained in the measurement, a new measurement is performed, after investigation, two stage nested analysis of variance is applied to estimated individual variation

A state of uncertainty where some possible outcomes have an undesired effect or significant loss as a risk quantitative uses of the terms uncertainty and risk are fairly consistent from fields such as probability theory, actuarial science, and information theory. Some also create new terms without substantially changing the definition of uncertainty or risk.

2.3.2 Procedure of uncertainty evaluation

Evaluation of measurement uncertainty by ISO-GUM recommendations can be summarized in the following step

1. Estimation of the standard uncertainties of the main sources: Definition of the quantity being measured data by the sensitivity coefficient
2. Calibration of the components of uncertainty for each main sources::
3. Calibration of the effective degree of freedom of the standard combined uncertainty
4. Calibration of the expand uncertainty: However, the ISO-GUM approach exhibits some limitations:
5. Model linearization: The principle of error propagation applied to obtain the standard uncertainty truncates the Taylor's series expansion in first order terms. This is a linear approximation that in some cases could need terms of higher order.
6. Assumption of normality of measurand in common practice, the distribution of the result is taken as normal and consequently, expanded uncertainty Ue is calculated as the product of the coverage factor k and the combined uncertainty Uc.
7. Record the data evaluated for uncertainty in an open document

2.3.3 Standard uncertainty

It performs operation of assurance by ISO-GUM in order of standard uncertainty U, Uncertainty is expressed standard deviation. Standard uncertainty Us is obtained MCMC of process .in Fig.3. Us is defined "Uncertainty of the result x of a measurement expressed as a standard deviation" by ISO/BIPM guide 98.

2.3.4 Combined standard uncertainty

The combined standard uncertainty Uc is adding many standard uncertainties Us of fault elements. Uc is defined "Standard uncertainty of the result y of a measurement when the result is obtained from the values of a number of other quantities". by ISO/BIPM guide 98.

Existence of two or more fault elements will use the multivariate analysis of supplement 3 in ISO-GUM. Each element is sampling as uncertainty elements (s_1, s_2, s_n).

$$Uc=\sqrt{U^2s_1+U^2s_2+\bullet\bullet\bullet+U^2s_n}\,, \tag{4}$$

2.3.5 Expand uncertainty

A expand standard uncertainty Ue for assurance performance is calculated as multiple factor by numerical coverage factor k to combined uncertainty as (5). Factor k is called coverage factor.[3] An assurance value is authorized by the final expand uncertainty Ue [11][13].

$$Ue=k*Uc \tag{5}$$

2.3.6 Coverage factor

The coverage factor.[3] is computed it by Welch-Satterwaite formula as (6) with Effective Free Degree (EFD) that is shown (V_{eff}). Free degree is important the number of samples based on maximum likelihood method. It is improved an (Akaike) information criterion (AIC). k is defined "Quantity defining and interval about the result of a measurement that may be expected to encompass a large fraction of the distribution of values that could reasonably be attribution to the measurand." By ISO/BIPM guide 98.

If the measurand distribution is approximated to a student's distribution, k is taken as the tabulated Student's t-value for given significance level. In the general cases, the analytical evaluation of the EDF is still an unsolved problem, in type B, generally contributing with infinite degree of freedom.

$$V_{eff}=\frac{u_c^4(y)}{\sum_{i=1}^{N}\frac{c_i^4u^4(x_i)}{v_i}} \tag{6}$$

An example, the use of a value of *k* other than 2 is taking k, equal to a t-factor obtained from the *t* -distribution when Uc has low degrees of freedom in order to meet the dictated requirement of providing a value that defines an interval having a level of confidence close to 95 percent.

3. ISO-GUM and assurance

ISO-GUM was legislated in enforcement an QA based on Quality Engineering (QE).

The standardization of measurements is high priority in laboratory medicine, its purpose being to achieve closer comparability of results obtained routine measurement procedures. The GUM has been increasingly adopted as a de facto standard procedure by calibration

laboratory,(see ISO17025). The GUM-GUM has been formally adopted as a US National Standard in the form of ANSI/NCLS Z540-2-1997, ISO is edited ISO-15189 to medical use.

3.1 To apply the ISO-GUM

GUM approach two main assumption must hold (12).

1. The system is modeled using a functional relationship between measured quantities X=f(x) and the measurements result y in the form y=f(x). The adequacy of the formula for uncertainty carried out u(y) which is derived by propagating uncertainties in a first-order approximation to the model of the measurement system. Production of analysis model is explained to the supplement 2.
2. The distribution of y is known, e.g. Gaussian or student distribution in order to obtain the value of coverage factor k for gaiting assurance interval with result.

3.2 Type A uncertainty estimation

Type A evaluation of standard uncertainty may be based on any valid statistical method for treating data. Example is calculating the standard deviation of mean of a series of independent observation, using the method of least squares to fit a curve to data in order to estimate the parameters of the curve and their standard deviations is calculated.

Type A is defined "Uncertainties are evaluated by the statistical analysis of a series of observation" by ISO guide. In type A, that performs only normal probability distribution of measurement data, and parametric test method is useful ANOVA, so called classical statistics. The normal distribution is also called the Gaussian or the bell shape curve, it is ubiquitous in nature and statistics useful the central limit theorem. Every variable element can be modeled as sum of many small variations which are approximated normal distribution. it is the only stable distribution having all of its moment finite.

3.3 Type B uncertainty estimation

Type B is upgrading evaluation of uncertainty than type A for abnormal distribution in order to obtain assurance, it needs employs other method than the statistical method, and based on non-parametric test method. The other method than statistical was proposed MCMC to type B. Type B is defined "Uncertainties evaluated by means other than the statistical analysis of a series of observations." in ISO/BIPM guide.

Assignment of PDF to a quantity analysis is using the Principle of Maximum Entropy (PME). Therefore the PME tells us that the Assignment of PDF is rectangular, t-distribution and normalize distribution. (see Fig.3). Type B evaluation of standard uncertainty is usually base on scientific judgment using all information available. Type A evaluation of uncertainty based on limited data are not necessarily more reliable than soundly based Type B evaluations.

3.4 Gibbs sampling by Bayesian theory

Gibbs sampling is an algorithm to generate a sequence of samples from the joint probability distribution of two or more random variable. The purpose of such a sequence is to

approximate the joint probability distribution, or to compute an integral (such as an expected value). Gibbs sampling is a special case of the M-H algorithm, and thus an example of practical use is MCMC algorithm. The algorithm is named after the physicist J.W. Gibbs, in inference to an analogy between the sampling algorithm and statistical physics. The algorithm was devise by brothers Stuart and Donald German, some eight decades after the passing of Gibbs.

Gibbs sampling is applicable when the joint distribution is not known explicitly, but the conditional distribution of each variable is known. The Gibbs sampling algorithm generates an instance from the distribution of each variable in turn, conditional on current values of the other variable. It can be shown that the sequence of samples constitutes a Markov chain and the stationary distribution. Markov chain is just the sought after joint distribution. Gibbs sampling is particularly well adapted to sampling the posterior distribution of a Bayesian networks, since Bayesian networks are typically specified as a collection of conditional distribution. The point of Gibbs sampling is that given a multivariate distribution, it is simpler from a conditional distribution than to marginalize by integrating over a joint distribution.

It is now the definitive document supplement of ISO-GUM on evaluating.

3.5 Assurance proceed

Quality Assurance (QA) of a measurement result is substantial by proposal new almost every year, QA is doing its best also in the field of a clinical examination to be able to respond to a patient or a donor effectively. The assurance performance of ISO-GUM is come out by set up of the confidence interval [4] and is decided. Therefore, it is considered that the value acquired by regulation of ISO-GUM is an assurance performance. ISO-GUM is edited in series to 98-5 from 98-1 as a guide of ISO/IEC. It has published by Joint Committee guide Measurement (JCGM). JCGM document number is JCGM 100-107.And ISO14253 [10] was publish as ISO standard.

ISO14253 (See Fig.4) contains decision rules which require the tolerance zone to be reduced by the measuring uncertainty. The measurement data are made to prove conformance a specification and expand by the measuring uncertainty. And it is attempting to prove non-conformance to a specification. It has known the legal phrase “prove beyond a reasonable doubt”.

Specification has two clear limits lines. Uncertainty makes the question of conformance more complex. In a drawing specification, it is usually clear what the limits tolerance are, it may be a maximum acceptable cover factors value of upper limit and a low limit is reject line.

The method of setting up a confidence interval (zone) is defined by ISO-14253-1 as same as conformance zone. And measurement uncertainty is increased.[14]

However, the ISO-GUM approach exhibits some limitations, like:

1. Model linearization: The principle of error propagation applied to obtain the standard uncertainty truncates the Taylor’s series expansion in first order terms. This is a linear approximation that in some cases could need terms of higher order.

2. Assumption of normality of measurand (z): In common practice, the distribution of the result is taken as normal and consequently. Expand uncertainty U(e) is calculated as the product of the coverage factor k and the combined uncertainty U(c). Thus k=2 is very commonly declared value, which corresponds to a level of significance of the approximately 95% in 2 sigma zone.
3. In calibration of the effective degree of freedom. If the distribution of z is approximated to a student's distribution, the coverage factor k is taken as the tabulated Student's t-value for given significance level and effective degree of freedom calculation by the Welch-Satterthwaite equation (6). In the general cases, the analytical evaluation of the effective degree of freedom is still an unsolved problem, type B uncertainties, generally contributing with infinite degree of freedom. However, the ISO-GUM 95 approach exhibits some limitations.
4. Modern concept of evaluation of measurement result uncertainty is based on the model function. Model linearization, the principle of error propagation applied to obtain the standard uncertainty truncates the Taylor's series expansion in first order terms. This is a linear approximation that in some cases could need terms of higher order as $Y=f(x_1,x_2,\ldots,x_i)$ as Eq.(1).
5. Eq.(1) applied to the use base on a first-order Taylor series expansion is approximation. Uc is gotten by doing a geometric mean of the type A and B result. This is model with one output which is adopted in current ISO-GUM. Knowledge of input quantities, which is compete, comes from their PDF. While the PDF has good theoretical foundations, the process of measurement modeling does not yet have them. There are no clues about it in the ISO-GUM. This is depended on experience data and prior knowledge.

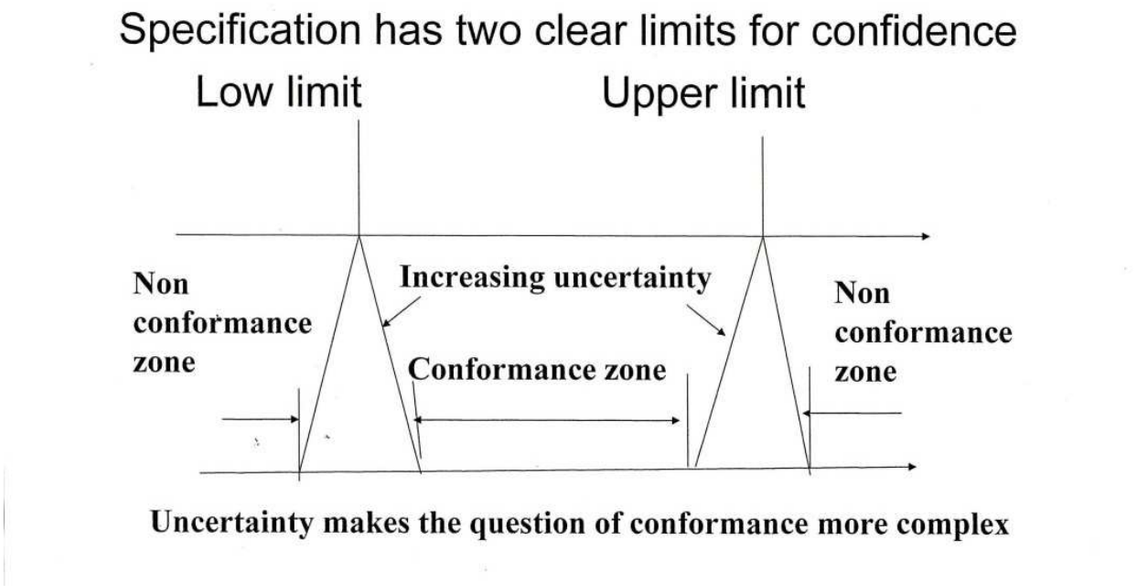

Fig. 4. Assurance interval by ISO-14253-1

If the measurand in expand uncertainty goes into a conformance (confidence interval or confidence zone), it value will be authorize the final report value as assurance performance.

4. Supplement of ISO-GUM

4.1 List of supplement

The list of supplements of ISO-GUM is shown below. (The mark * is under plans).

Introduction to the GUM related documents, there were published already three supplements.

1. Supplement1: Numerical methods for the Propagation of distributions using a MCMC method [3] by document JCGM101.
2. Supplement 2: Extension to any number of output quantities is useful models. JCGM102.
3. Supplement 3: Modeling for useful multivariable analysis. JCGM103.

An introduction to the GUM is under planning documents of supplement for ISO-GUM, there are four supplements (3).

4. *Supplement 4: An introduction to be GUM and related documents. Published 2009 JCGM104.
5. *Supplement 5: Concepts and basic principle of measurement uncertainty evaluation.
6. *Supplement 6:The role of measurement uncertainty in deciding conformance to specified requirements.
7. *Supplement 7: Application of the least squares method.

Data Quality Assurance Object (DQAO) development process consists of the following seven steps by supplement 4.

Step 1. State the Problem
Step 2. Identify the Decision
Step 3. Identify the Inputs to the Decision
Step 4. Define the Study Boundaries
Step 5. Develop a Decision
Step 6. Specify Acceptable Limits on Decision Errors
Step 7. Optimize the Design for Obtaining Data.

4.2 MA in supplement 3

Practical use of multi-variable analysis (MA) is required for BCA from two or more uncertainty elements being inherent. MA is defined in supplement 3. As for an algorithm, the theoretical formula (3) is usefully. The supplement 7 is considering using a least squares method as a base and using Burgers Equation and Crank-Nicolson method for a MA Propagation of uncertainty for several variable can be simple considerably if it is simple multiplicative of secondary variable.

QA of a measurement result is substantial by proposal new almost every year.

The practical use of MA is required for BCA from two or more uncertainty elements. It is expected that the analysis result can begin to find a new uncertainty factor.

5. Measurement principal

5.1 Radio-Immuno Assay (RIA)

The experiment should be use test reagents of RIA that is a kind of BCA. RIA is a scientific method used to test antigen (example, hormone levels in blood) without the need to use a bioassay. It involves mixing known quantifies of radioactive antigen with cold antibody to that antigen, then adding unlabeled (cold antigen) is measuring the amount of labeled antigen displaced. Initially, the radioactive antigen is bound to the antibody. When cold antigen is added, the two compete for antibody binding sites. The bound antigens are separated from unbound one. Radioactive isotope is used gamma emit of I-125. This is both extremely sensitive and specific, but it requires special precaution because radioactive substances are used, sophisticated apparatus, and is expensive. In this research, it is useful main data of Erastrse-1 regent which is a sort of pancreas hormone.[22]

Immunoassays are a form of macromolecular binding reaction; no covalent chemical bonding is involved. Antibodies interact with their antigen by weak hydrogen bonding and van der Waals force. Antigen-antibody reactions are dependent on complementary matching shapes being assumed by antibody variable regions of the immunoglobulin. Almost all polyclonal antibodies used in immunoassay reactions are of the immunoglobulin G class. The N-terminal 110 amino acid residues of both the heavy and light chains of the immunoglobulin molecules are variable in sequence and interact to form the antigen binding site. Nevertheless, this variability gives rise to a vast array of difference antibodies binding to different molecules. Attributes of an ideal immunoassay is shown to follow

1. The immunochemical reaction behavior should be identical and uniform for both the inference preparation and the analysis in the homogeneity sample.
2. The immunochemical reaction of the antibody reagent is uniform from batch to batch.
3. The immunochemical method is well standardized to ensure that the size of measurement signal is caused only by the antigen-antibody product.
4. For macromolecules the results are declared in arbitrary unit, i.e. international Unit (IU) conversion to mol/L(SI) unit is constant and is dependent on many factors.

The immuno-reaction of an antigen and a catalyst (an antibody activity) is led to measurement theory of RIA with reaction kinetics. Reaction kinetics is expressed with the chemical equivalent amount compound by unit time t. The chemical reaction is shown in Fig 5. The process of chemical change is divided into three phases that are a signs phase at growth phase and stagnation phase. A signs phase shows the resistance characteristic over a reaction in the preparation step of a reaction. A growth phase shows reaction capability in the stage where a reaction grows rapidly. A stagnation phase with asymptote which is a stage where the chemical reacting finally and reaches a chemical equilibrium. An uncertainty element can be expressed with the abnormal state of reaction time and reaction capability.

The strength of binding is determined by equilibrium binding constant for the antigen-antibody complex formations. The binding follows the basic thermodynamic principles with reversible reaction between two molecules. This relationship is described by the chemical reaction model as (7) which is useful a chemical kinetics reaction R_1 of immunity with a reversible reaction R_2 in a polynomial expression.

$$P+P^*+Q \underset{R_2}{\overset{R1}{<=>}} P^*Q+PQ+PI+P^*I \rightarrow P^*Q \quad (7)$$

Where are:

- P: antigen,
- Q: antibody,
- P*: Labeled antigen with detectable marker,
- PQ: Reaction compound,
- P*Q: reaction compound with P*,
- $R_{1,:}$ association constant
- R_2: disassociation constant
- R; affinity.(Binding ratio P*Q/Po= %)
- Po is total antigen Po=PQ+P*Q+PI+P*I
- PI: Abnormal reaction compound.

Po is invariably an usual constant of nature in the "law of mass action". In this case, it must be the measured P*Q/Po of the effective binding ratio. Affinity is the same as the kinetic reaction rate. An affinity increases until the deactivation of saturation that the reaction is based in the reaction process in time. Kinetic chemical reaction is accelerated by bio-materials as a quadratic differential polynomial equation with reaction time t. The secondary order differential equation is as follows according to three phases as (8)

$$Ad(P^*Q)^2/dt_2+Bd(P^*Q)/dt+C(P^*Q) \quad (8)$$

The extent of reaction is shown in Fig.5. Secondary order differentiation of the first item shows the rate of acceleration included a special resistance phase. It is shown to the portion of start of the reaction curve in Fig.5. A primary differentiation of the next item is shown reaction velocity. The last item shows the amount of chemical compound after reached chemical equilibrium as stoichiometry. The first item has role important for security of reaction and the analysis of an outlier.

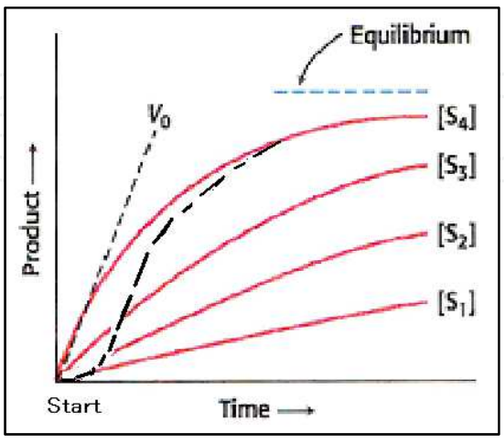

Fig. 5. Elastase-1 chemical reaction

Kinetic reaction ratio is estimated as follow

$$d[P^*Q]/dt=R1[P^*][Q]-R2[P^*Q]\ldots \quad (9)$$

$$k1[P^*][Q]=(R1-R2)[P^*Q]\ldots\ldots\ldots\ldots \quad (10)$$

The final reaction a stagnation phase is reached on chemical equilibrium. It become to $d[P^*Q]/dt=0$ and change from (9) to (10). An affinity state is shown on the reaction curve at time.

5.2 Calibration curve

In this research, a purpose is improving the accuracy of the calibration curve used for quantitative analysis and making it level which can be assurance. The accuracy of calibration curve is important as intermediate accuracy of the whole measurement system. The measurement data was collected by equalization of double sample in order to make high order accuracy. The Data Quality Object (DQO) of the improvement accuracy targeted the calibration curve for a chemistry quantity analysis.

Even in the case of measurements requiring multipoint linear (non-linear) calibration with five or more different concentration reagents of reference homogeneity material. The uncertainty of routine test values can be quantified using basically the same procedure as "Estimating the uncertainty of routine test values" except that the uncertainty of the reference material is calculated as a combined standard uncertainty using the mean value obtained by averaging the standard uncertainty (see to Fig.6).

The reference material used should be an actual sample, the property of which is similar to the patient spaceman to be assayed. Even in the multi-point linear calibration with three or more different rations concentrations of reference material, the uncertainty of routine test values can be quantified using basically procedures. Test reagent is called calibrator.

All the product calculation curves are having the quality verified by formula of Mechaelis-Menten formula.

Key aspect is the Antigen-Antibody interaction.

1. Reaction is reversible and favors complex formation under physiological condition.
2. Binding depends on hydrogen bonds, van der vaals forces, ionic bonds, hydrophobic interaction.
3. Binding is very specific and requires the correct 3-D structure of an antigen.
4. The amount of complex formed depended on concentration of antibody and antigen. Both antigen and antibody (if large enough) have multiple sites for binding to occur. Therefore, extensive cross-linking can occur when both are present in solution. When antibody and antigen reach equivalence large immune complexes form which can precipitate out of solution.

6. Experiment method

6.1 Progress of work

In immunochemical analysis can be nonlinear analysis that is applicable of estimating to the uncertainty of assigned value of calibrators and QA control sample.

The purpose of such a sequence is to approximate the joint probability distribution, or to compute an integral (such as an expected value). The estimation of a possible discrepancy takes into account both random error and in the measurement process. The distinction to keep in mind and with regard to be able corrected or cannot be corrected theoretically least.

Gibbs sampling is particularly well adapted to sampling the posterior distribution of a Bayesian networks, since thus are typically specified as a collection of conditional distribution. The point of Gibbs sampling is that given a multivariate distribution, it is simpler to sampler from a conditional distribution than to marginalize by integrating over a joint distribution. The algorithms are useful Softcomputing method, fundamental statistical method, MCMC and MA, Softcomputing method is fuzzy function and chaos function.

6.2 Data quality object(DQO)

This experiment used the test reagent kits of the Elastase-1 that is one of test reagent of pancreas hormone mainly. The test method is RIA [17], RIA is a kind of BCA with detectable marker that is labeling the radioactive material of I-125. A measurement method is detection of the gamma ray which I-125 emits.

The calibration curve made of the test reagent of six sorts of concentration (dose) that is the arrangement harmonious in the shape of a stairs state. A calibration curve is created by applying regression analysis to a frequency density of measurement result. The composition of reagent concentrations are six sorts of 50, 150, 500, 1500 and 5000 dose. Dose is international catalyst unit (IU). Test reagent is called as calibrator. The number of sample size is total 320 sets of calibrators that is divided three groups (lots) that consists one group of 120 sets and two groups of 100 sets. The number of one group is recommended the least in ANOVA. It was made three groups here in order to investigate whether a difference exists between groups. Fig.6 shows the procedure which creates distribution of statistics from the population calibration curves to which regression analysis was applied the frequency density distribution is created by measurement data and analyzed. In an immunoassay the total amount of antigen for standard solution is known by each dose. Plotting affinity against total antigen produces the standard curve. The value for affinity is determined by radioactivity amounts remaining bound divided by the total amount of radioactivity added in the beginning. The radioactivity is proportional to the concentration of the labeled antigen. It is using this standard curve and the affinity for an unknown sample the antigen concentration can be calculated. The dose response curve shown is that a typical of RIA standard curve that is used calibration curve.

In an immunoassay the total amount of antigen for standard solution is known by each dose. Plotting affinity (binding ratio) against total antigen produces the standard curve. The value for affinity is determined by radioactivity remaining bound divided by the total amount of radioactivity added in the beginning – the radioactivity is proportional to the concentration of the labeled antigen. It is using this standard curve and the affinity for an unknown sample the antigen concentration can be calculated. The dose response curve shown is that a typical of RIA standard curve.

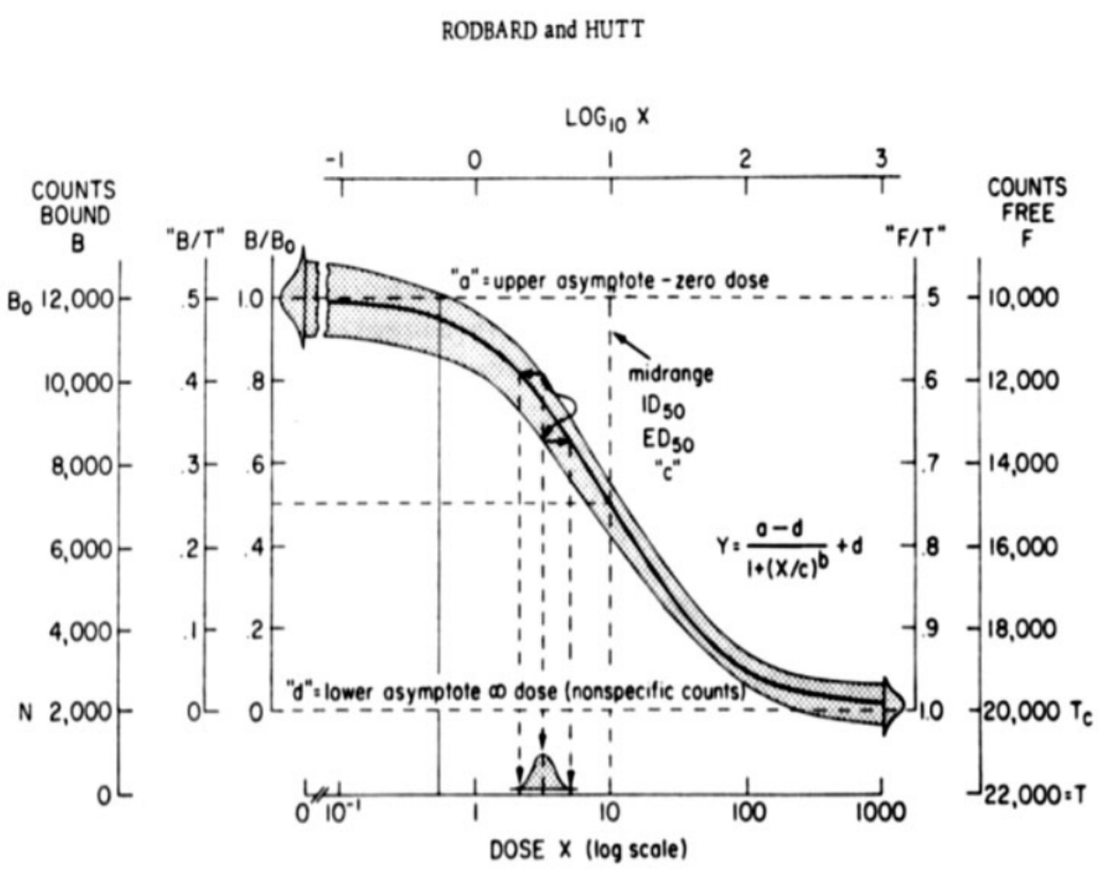

Fig. 6. Make a probability distribution of Calibration curve batch, for QC[16].

6.3 Additional reagent samples

In this experiment, Elastase-1 sample data is verified whether it would be added other test regents of two homeopathic test reagents of the same usage RIA and test chacking.. Furthermore, in order to investigate an information criterion number and likelihood test and it used multivariable analysis in the time series.

Two sorts of homeopathic reagents having chosen, there are Thyroxin, and Testosterone.

The reagent of Testosterone is one female hormone and the composition of reagents concentrations are 6 sorts dose which are 25, 50, 100, 250, 500 and 1000. The reagent of Thyroxin is one of thyroid hormone and the composition reagent concentrations are 5 sorts dose which are 0, 3.0, 6.0, 12, and 24.

7. Experiment result

7.1 PDF data of elasyase-1 reagents

Measured data is shown in Fig.7 and Fig 8. Both figure quotes the pareto graph that is a pile of the quasi normal distribution curve (solid curve B) on the measured PDF graph (bar graph A). Fig.7 shows 0 dose reagents data as the largest affinity in six sorts of calibrators of

reagent, Fig.8 shows 5000 dose reagent data as the lowest affinity in the six dose sorts. A bar data serves as basic data from now on advancing analysis which is observation data as A in Fig.7 and Fig.8.

Quasi normal distribution is created by regression analysis from the measured frequency distribution as B in Figs.7 and Fig.8. The ordinate shows the account of frequency density of total 320 sample sets. The abscissa shows affinity (%) divided into 20 steps between maximum and minimum affinity.

PDF graph is carrying out random change in any range of sample groups. The PDF of random variation exists completely characterized in both figures.

Both figures are chosen as example of representation from six dose data. Six sorts all concentrations of PDF data were shown the abnormal distribution. All PDF data of measurement results of six sorts were not same as the form. Abnormal distributions are cannot computed both skewness and kurtosis.

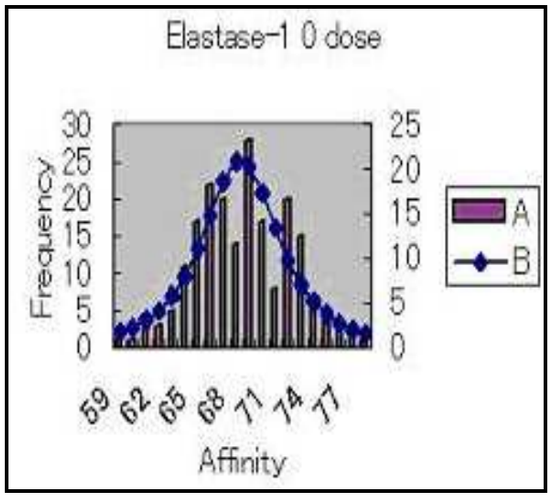

Fig. 7. PDF of 0 dose data of Elastase-1

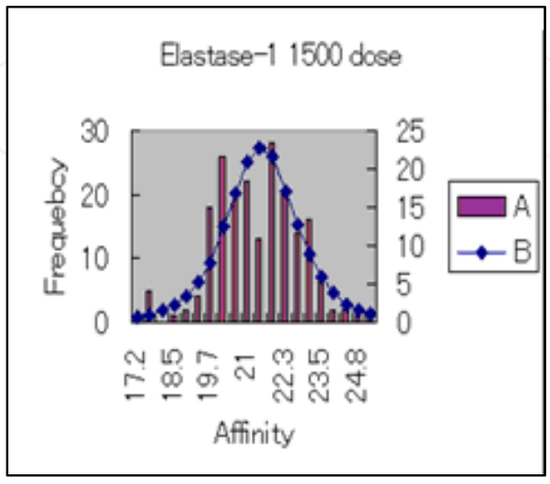

Fig. 8. PDF of 5000 dose data of Elastase-1

7.2 The superposition graph of six PDF data

Fig 9 is shown a superposition graph by six measured PDF forms on the variation of affinity (%) of maximum and minimum positions. All of PDF are shown not same form.

Fig.10 is shown a superposition graph the abnormal distribution of six sorts curve obtain by regression analysis, because all distributions are not take same as peak position.

The ordinate is the account of frequency of total 320 sample sets. The abscissa is shows affinity (%=P*Q/P_0). The abnormal PDF distribution should be required to create the CDF follow up MCMC.

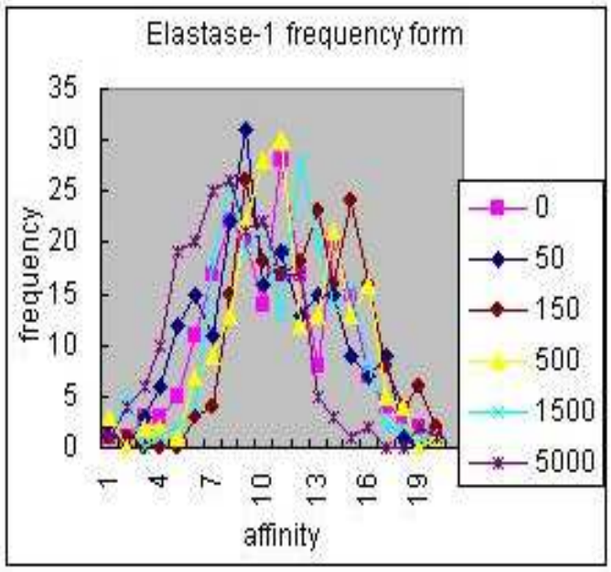

Fig. 9. A superposition graph of six measured PDF.

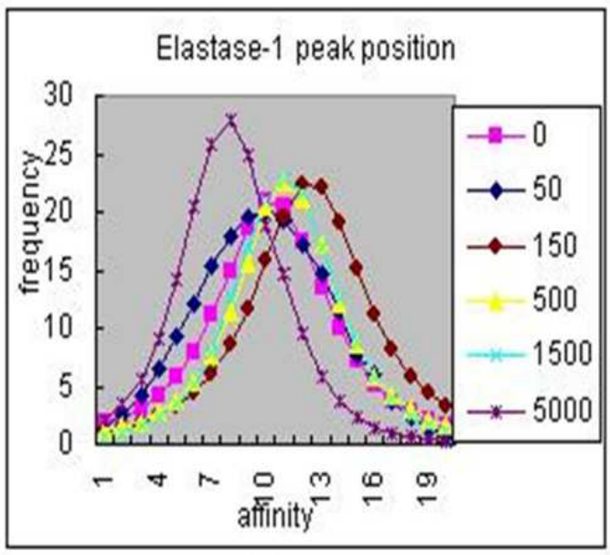

Fig. 10. A superposition graph of six the abnormal PDF.

7.3 fundamental statistics quantity

Table 2 shows what summarized the fundamental statistics quantity (AIC, mean, RSS, Medi, peak, Max, Min, F-test and t-test) and the data of EDA added the operation result by chaos theory and Fuzzy logic. Max is the maximum value in upper limit of confidence interval and Min is the minimum value in the lowest limit of confidence interval. Max and Min data use primary confidence interval. Fuzzy logic use also 20 steps member function in fuzzy logic, Chaos theory use difference equation in nonlinear.

Some value shows the same value based on many columns in table 2. Six columns (Fuzzy, AIC, mean, RSS medi and peak) are shown in red bold letter. The focus inside of the same value is the mean. The mean value can be referenced as a central value by data in this experiment. This value can be set as a reference value by Type A for internal quality control (IQC). The assurance interval by type A was calculated by 95% level and coverage factor k=2. It is 2 sigma of a routine test level and it can be assurance against 95% level which is given by the 0,025 and 0.975 fractions limited [7]. If measured data is over the limited line, it is unclear that dispersion is large, so that the affinity was a low value.

Dose	0	50	150	500	1500	5000
Chaos	71.84	65.94	54.93	36/.77	22.5.2	12.17
Fuzzy	**68.5**	**61.8**	**52.1**	**34.8**	**20.7**	**10.4**
AIC	**68.46**	**62.42**	**53.0**	**34.97**	**21.34**	**10.59**
mean	**68.4**	**61.8**	**52.2**	**34.7**	**20.8**	**10.5**
RSS	**68.3**	**61.9**	**52.1**	**34.7**	**20.7**	**10.4**
Medi	**68.3**	**61.7**	**53.1**	**34.8**	**20.6**	**10.4**
peak	**68.3**	**62.2**	**52.1**	**34.9**	**21.5**	**10.6**
Max	78.2	71.8	60.0	43.1	28.9	17.1
Min	46.7	41.1	34.4	21.7	12.4	6.9
F-test	2.17	2.16	2.17	2.17	2.17	2.17
t-test	2.03	2.02	2.03	2.03	2.03	2.02
EFD	0.18	0.17	0.19	0.17	0.17	0.18

Cipher cod of result
Chaos chaos theory: Difference equation in nonlinear
Fuzzy: 20 steps membership' function
AIC: Likelihood function (Akaike Information Criterion)
RSS: Root Sum Square
Medi: Central value
Peak: peak point.
Max: Maximum value in distribution
Min Minimum value in distribution
F-test F-distribution
t-test t-distribution
EFD: Effective Freedom Degree

Table 2. Fundamental statistics quantity by type A

7.4 CDF data

CDF data shows in Fig. 11 and Fig 12. These data quoted a pareto graph that is a pile of CDF distribution curve (solid curve B) on the PDF (bar graph A). Fig.11 shows the data on 0 dose reagents as the largest affinity in six sorts of reagent, and Fig.12 shows the data on 5000 dose reagent as the lowest affinity in six sorts of reagent.

This research analyzed of abnormal portion looked on CDF curve in Figs.11 and 12. By ISO-GUM of type B. it acquire further higher measurement accuracy and, it is required to analyze a fault element by FTA and EDA. Here, it has to process by type B for abnormal distributions. Fig 7 and Fig,8 data was useful basic data in this research. In both Figs 11 and 12, the reagent kit is divided into three groups (lots) and it shown influence to verify of difference between in reagent kits. The ordinate of is the account of frequency of total 320 sample sets. The abscissa is shows affinity (%=P*Q/P_0) which All graphs quote variation of affinity that divided the affinity into 20 ranks between maximum and minimum. The ordinate quotes generating frequency counts.

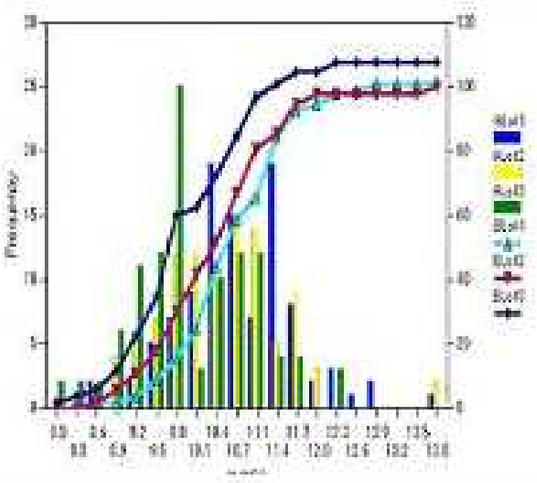

Fig. 11. Elastase-1 0 dose of 3 rots graph.

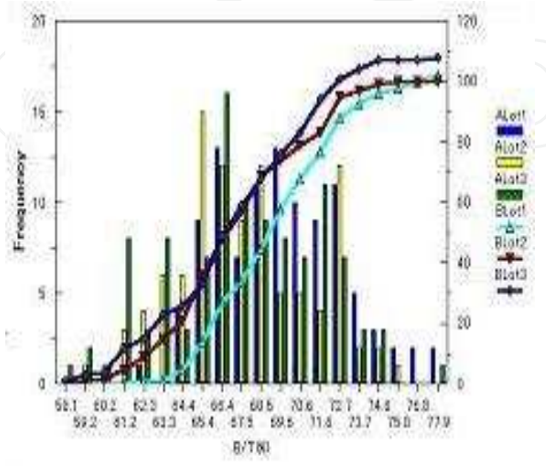

Fig. 12. Elastase-1 5000 dose of 3 rots graph

The CDF curve shown the form of sigmoid and bending has seen in some portion. The bend of a curve suggested that abnormalities existed in a chemical reaction.

All of CDF result (including the four sorts of other dose) showed a state of an abnormal distribution similarity and not same form. The abnormal distribution of PDF should be required to useful MA that is nonparametric test and nonlinear analysis.

7.5 Confidence zone (interval)

The protocol of QA was development to estimate the uncertainty of measurement of a chemical analysis by utilizing in house validation studies. The approach was to generate an estimate of the uncertainty across the analytical concentration range. [21]

Table 3 shows amount of calculation result by the Welch Satterthwaite as Eq (3) for coverage factor simulation. Value in table 3 is converted into an effective free degree from the Welch Satterthwaite factor by standard statistical table showing EFD in table 3. The experiment result needs to set coverage factor k to 2.2 by standard statistical table. Because coverage factor 2.0 is generally used as standard. It is necessary to make narrower than a general value the confidence interval which can be assured in this case.

Table 4 shows the confidence interval and related data for QA, a result is expressed numerically and it is. Assurance Interval (AI) data shows final assurance value. Reject zone is shown also in the t-distribution and the square distribution in MCMC of Fig.3.

The assurance interval (zone) determined based on type B of ISO-GUM, in this case is required to set the narrower interval than getting ANOVA value for external quality control (EQC) that is required 99.7% as more than three 3 sigma. Only the measured value which exists inside an assurance interval turns into assured performance.

The measurement vale whose assurance is attained only a mean value which is exist in the confidence zone (see Fig 2) inside assurance interval (AI in table 4) that is authorize.

In the case of a type A evaluation of uncertainty, repeated measurement indications are regarded as independently drawn from normalized frequency distribution and according to its suggestion the uncertainty evaluation method of supplement 1 is applied after having assigned scaled and shifted t-distribution to corresponding input quantities.

Next research investigated the cause of the abnormal part shown in curve of CDF. FTA and RCA performed the method.

Sample size	0	50	150	500	1500	5000
102	17.18	16.83	16.28	16.62	16.64	18.22
100	18.22	16.87	16.28	16.45	16.88	16.84
110	18.27	18.27	18.68	16.07	18.19	18.51
29	7.31	7.44	7.3	7.31	7.27	7.29
341	60.98	59.39	64.24	56.45	58.97	34.1

Table 3. Calculation result by the Welch Satterthwaite

	Dose	0	50	150	500	1500	5000
SD	Central	62,4	56.4	47.2	32.4	20.6	12.0
	0.95 UA	8.64	8.43	7.03	5.86	4.53	2.8
	CIA	53.8 71,0	48. 64.9	40.2 54.2	26.5 38.3	16.1 25.2	9.2- 14.8
N.D	Central	68.3	62.2	52.1	34.9	21.5	10.6
	0.95 UB	7.26	6.54	6.11	451	3.11	1.84
	CIB	61.- 75.6	55. 68.7	46- 58.21	30.3 49.6	18.4 24.6	8.76- 12.4
Us	UC	11.2	10.67	9.22	7.32	5.40	3.29
AI	CIC	**62.4 73.9**	**56.8- 67.7**	**4.61- 56.7**	**31.3 38.6**	**18.8 24.2**	**9.0- 12.2**

Cipher cod of result
SD: Standard Deviation
ND: Normalize Distribution
Us: Standard Uncertainty
AI: Assurance Interval
Central value
0.95UA: 0.95%x2 Uncertainty type A
0.95UB: 0.95%x2 Uncertainty type B
CIA: Confidence Interval type A
CIB: Confidence Interval type B
UC: Combine Uncertainty
CIC: Confidence Interval for assurance
UC: Combined uncertainty

Table 4. Accuracy interval and related data

7.6 MA date

7.6.1 Data of elastase-1

Uncertainty associated with measuring operation which are calibration dispersion, within-day and between days, within-laboratory and between- laboratory dispersion, and the like, including factor due to reagent preparation and instrument variation. In co-data which is inherent in a measurement result, two or more uncertainty factor analyze by MA. The time depended uncertainty analysis is day to day variance in this experiment.

In former research, it used multiple-regression for MA based on "Law of propagation of Uncertainty" in EDA and has found out a new uncertainty factor. Fig.13 and Fig.14 is importance data in which is new variable element as the influences for storage days. While the reaction capability is quoted fall down of a test reagent for storage days.

Fig.13 shows changing of the reaction capability by storage days of 0 dose reagent. Data of Elastese-1, it is data comes to deteriorates in right going down in proportion to the increase in days to day. To while the reaction capability of a test reagent downs for storage days.

Fig.14 shows changing of the reaction capability by the storage period days of 5000 dose reagent. Data shows a degradation of reaction capability that reaches a detectable limit and it is meaning the unstable state of large uncertainty.

In both graph, the ordinate is the affinity (%). The abscissa is shown storage days.

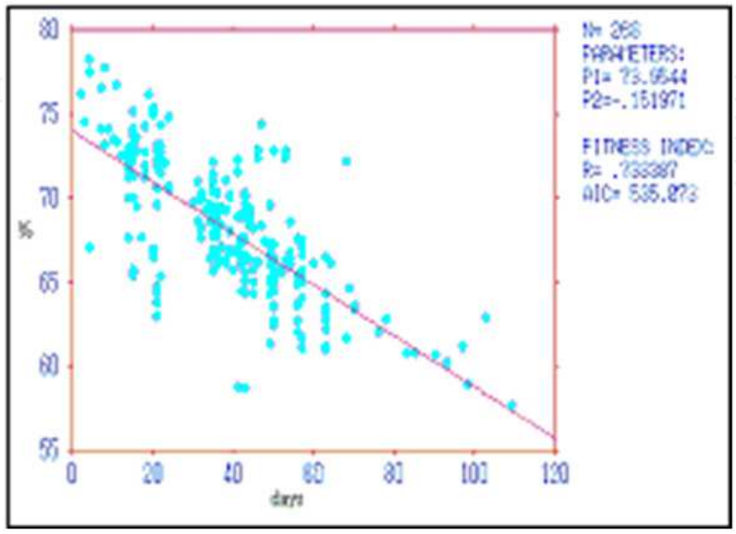

Fig. 13. Change under storage days of 0 dose.

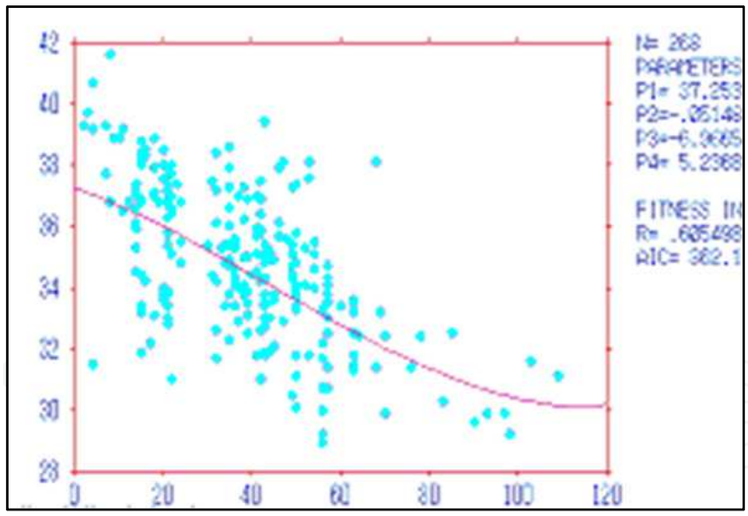

Fig. 14. Change under storage days of 5000 dose

Fig.15 is shown change of SD value under storage days by EDA. In Fig 15, SD value has fallen so that the concentration of reagent as which it is regarded the change united with the biorhythm of 28 diurnal periodicity exists. SD value with reaction capability is falling as to slide with concentration dose. Data of Fig.15 has mean very important to improved accuracy as fault elements The abscissa shows the storage days of every seven days interval in Fig.14. The change interval was a periodical target on the 28 days interval of biorhythm. In the addition, in the domain of low binding capacity, all the unstable of accuracy are as same.

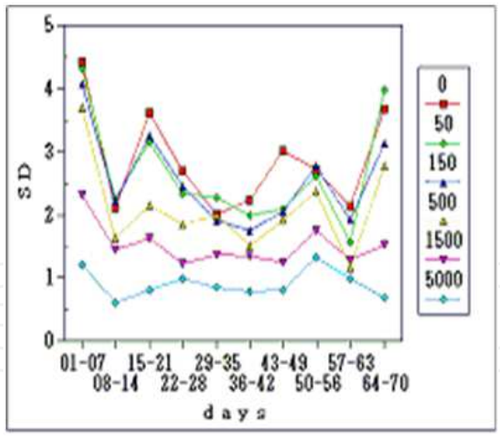

Fig. 15. Storage days variance by type B of EDA

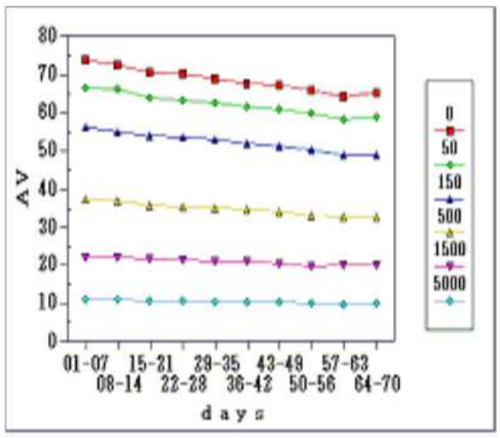

Fig. 16. Storage days variance by type A of ANOVA

Fig.16 is shown change of average value under storage days by the data based on ANOVA, only a flat change of right going down is shown and a periodic change is not seen.

7.6.2 MA data of additional reagents

In this experiment, since it seem that the data of 7.6.1 is important. I verified whether the same result would be obtained with two homeopathic test reagents of the same usage RIA. Furthermore, in order to investigate an information criterion sample number and likelihood test and it used multivariable analysis in the time series. The results are shown Fig.17 and Fig.18.

Fig.17 and Fig. 18 shows the graph which laid change of SD and of the number of samples on the top of storage days. Fig. 17 shows Thyroxin data. Fig.18. shows Testosterone data.

In both figure, although a periodic change is looked at by change of SD for under every storage days of six sorts dose as Standard Deviation (SD) in order to explore the root cause of fault elements, it will become unstable data few samples. The both figures showed the same characteristic results. Thereby, the check of the reproducibility of an uncertainty factor was completed. About the number of samples, it is the information criterion by maximum

likelihood theory need to be inquired. This research is under experiment. In Fig.17 and 18, it is unstable area by number of five or less samples. The ordinate shows SD and number of samples. The abscissa shows the storage days of every seven days interval. The ordinate shows SD and number of samples In both graph, the ordinate is the affinity (%) and frequency. The abscissa is shown every seven storage days.

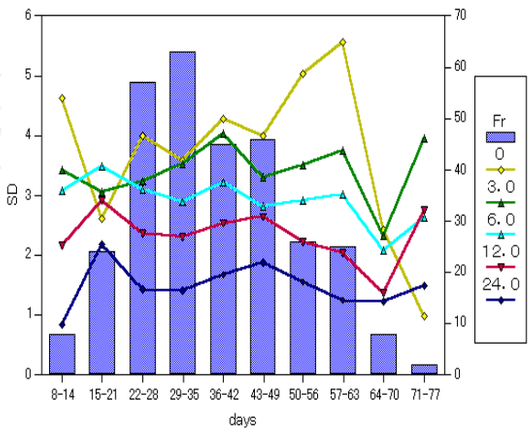

Fig. 17. Shows Thyroxin data.

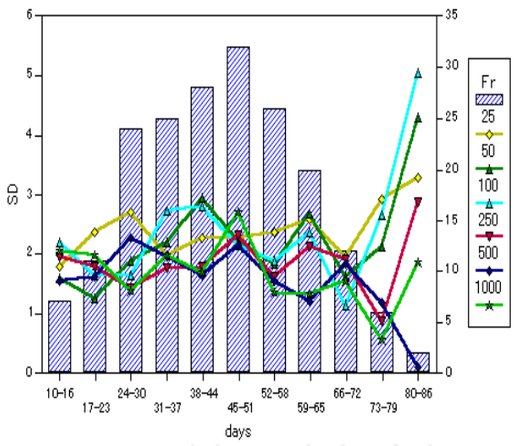

Fig. 18. Shows Testosterone data.

7.6.3 Interaction and allosteric effect in data

The purpose of this chapter is to outline methods for assessing uncertainties related to material inhomogeneous that can be a factor in uncertainty analysis (see chapter 6.2).

One more is found in the uncertainty factor. The interaction effect and the allosteric effect are generating by the source of biorhythm. Binding of antibodies to antigens is reversibly and very specific. The introduction of an immune response depends on the size of antigen. Small molecular weight compounds (<2000 Daltons) such as drugs is unable to induce antibody formation.

The interaction investigated the phenomenon prevented from fundamental reaction principle. The example of calibration curve has generating of an interaction which is shown

sample in Fig 19. The interaction and allosteric effect were considered by from the experiment results of in fig.19. Ordinate is affinity (%) of reagent. Abscissa is dose of reagent at table position as from 0 to 5000.

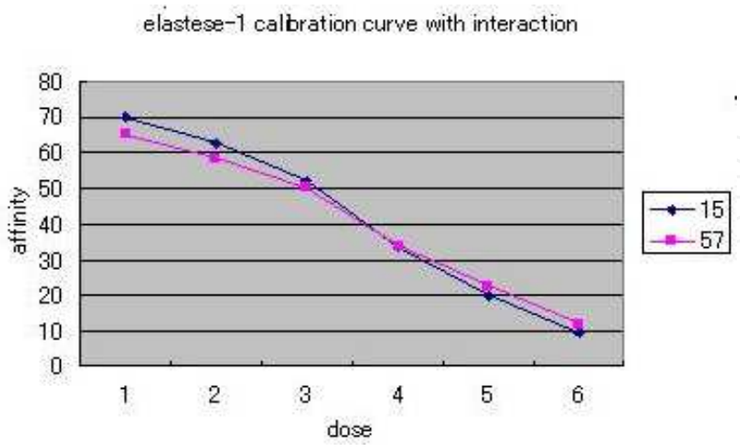

Fig. 19. Interaction is exact between 2 calibration curves as an example

Some one exists in the allosteric effect which inhabits reaction process. Both effects like in the bio- science on theorem of logistic function.

8. Conclusion

QA system of clinical test data by ISO-GUM is made utilization in 2006. It included in IT system plan for medical health care in 2010. This research is continued in order to reliance of QA further. In ISO-GUM it is pursued two or more buried multivariable uncertainty factors. Validity of ISO-GUM is increasing by additional issue many supplements.

This research started for the purpose of preventing the clinical misdiagnosis by ambiguity data on medical care. Therefore, the work is obtaining that of data stable in higher accuracy has been continued. Improve strategy found out by uniting QE and ISO-GUM. The assurance of measurement data which was able to be attained new technology for is main purpose. Clinical data obtained and expected from exact prediction of patient individual's pathological change. After that, a result came to be utilized for the world wider base medical care of EQAS when improvement of ambiguity was obtained. The result of research has been satisfied,

Uncertainty of measurement, traceability and numerical significance are separate but closely related concepts that affect both the format and information conveyed by a quantitative test result. In addition, use of SI units provides a consistent basis for the reporting of clinical laboratory. Katal as a SI unit which evaluates the reaction kinetics of chemical will be used for the near future.

The experimental result sees enable exact diagnosis decision taking in Bayes inference to QE and ISO standard. Medical Laboratory Quality System (MLQS) is essential in laboratory to the correct result for patient and donor by Good Laboratory Practice (GLP)

QA has grown to be equivalent QC which can obtain the same result when and anywhere.

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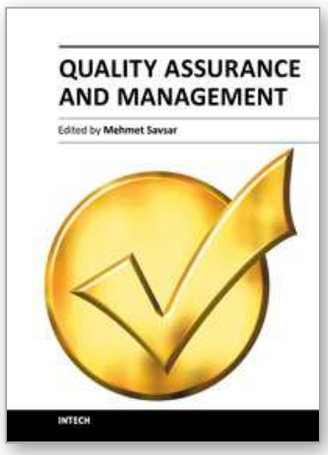

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The purpose of this book is to present new concepts, state-of-the-art techniques and advances in quality related research. Novel ideas and current developments in the field of quality assurance and related topics are presented in different chapters, which are organized according to application areas. Initial chapters present basic ideas and historical perspectives on quality, while subsequent chapters present quality assurance applications in education, healthcare, medicine, software development, service industry, and other technical areas. This book is a valuable contribution to the literature in the field of quality assurance and quality management. The primary target audience for the book includes students, researchers, quality engineers, production and process managers, and professionals who are interested in quality assurance and related areas.

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