カラム：内径 4.6 mm，長さ 15 cm のステンレス管に 5 μm の液体クロマトグラフィー用オクタデシルシリル化シリカゲルを充てんする．
カラム温度：40℃付近の一定温度
移動相：アセトニトリル/水混液（1：1）
流量：アモキノールの保持時間が約 X 分になるように調整する．
システム適合性
システムの性能：標準溶液 20 μL につき，上記の条件で操作するとき，アモキノール，内標準物質の順に溶出し，その分離度は XX 以上である．
システムの再現性：標準溶液 20 μL につき，上記の条件で試験を 6 回繰り返すとき，アモキノールのピーク面積の相対標準偏差は 1.0%以下である．

医薬品製造販売承認申請書　別添

（販売名：サクラ錠 30 mg）

式 1（純度試験）

各類縁物質の量（mg）= $W_S \times A_T/A_S \times$ X.XXX

W_S：アモキノール標準品の量（mg）

式 2（製剤均一性：RTRT）

相対標準偏差（%）=X/s×100

$$s=\sqrt{\sum_{i=1}^{n}(xi-\overline{X})^2/(n-1)}$$

X：x_1，x_2，・・x_nの平均値

x_1，x_2，・・x_n：試験した個々の試料に含まれる主薬含量

n：試験した試料の全個数

s：試料の標準偏差

式 3（製剤均一性）

アモキノールの量（mg）= $W_S \times A_T/A_S \times$ X.XXX

W_S：アモキノール標準品の量（mg）

式 4（溶出性:RTRT）

アモキノール（$C_{XX}H_{XX}N_XO_X$）の表示量に対する溶出率（%）

= 108.9 − 11.96×アモキノールの粒子径[$\log_{10}$(d(0.9))] − 7.556×10^{-5}×ステアリン酸マグネシウム比表面積（cm^2/g）−0.1849×滑沢剤混合時間（分）− $3.783*10^{-2}$×平均打錠圧（N）

式 5（溶出性）

アモキノール（$C_{XX}H_{XX}N_XO_X$）の表示量に対する溶出率（%）

= $W_S \times A_T/A_S \times V'/V \times 1/C \times$ X.XXX

W_S：アモキノール標準品の量（mg）

C：1 錠中のアモキノール（$C_{XX}H_{XX}N_XO_X$）の表示量（mg）

式 6（水分）

アモキノールの水分量（%）

=（試料の水分量（μg）−空試験液の水分量（μg））/本品 10 錠の質量（mg）

式 7（定量法：RTRT）

アモキノール（$C_{XX}H_{XX}N_XO_X$）の表示量に対する含量（%）

=＜第一工程＞混合工程における混合末中のアモキノール含量（%）×＜第三工程＞打錠後の錠剤質量（mg）/C

C：1 錠中のアモキノール（$C_{XX}H_{XX}N_XO_X$）の表示量（mg）

式 8（定量法：RTRT）

アモキノール（$C_{XX}H_{XX}N_XO_X$）の量（mg）= $W_S \times Q_T/Q_S \times X.XXX$

W_S：アモキノール標準品の量（mg）

式 9（定量法）

アモキノール（$C_{XX}H_{XX}N_XO_X$）の量（mg）= $W_S \times Q_T/Q_S \times X.XXX$

W_S：アモキノール標準品の量（mg）

添付資料

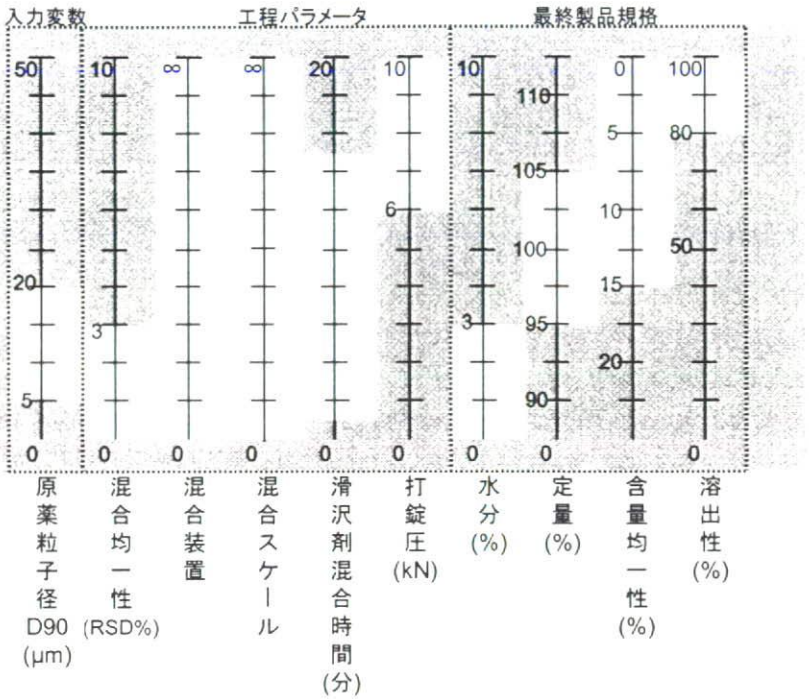

図 1（サクラ錠 30 mg のデザインスペース及び規格）

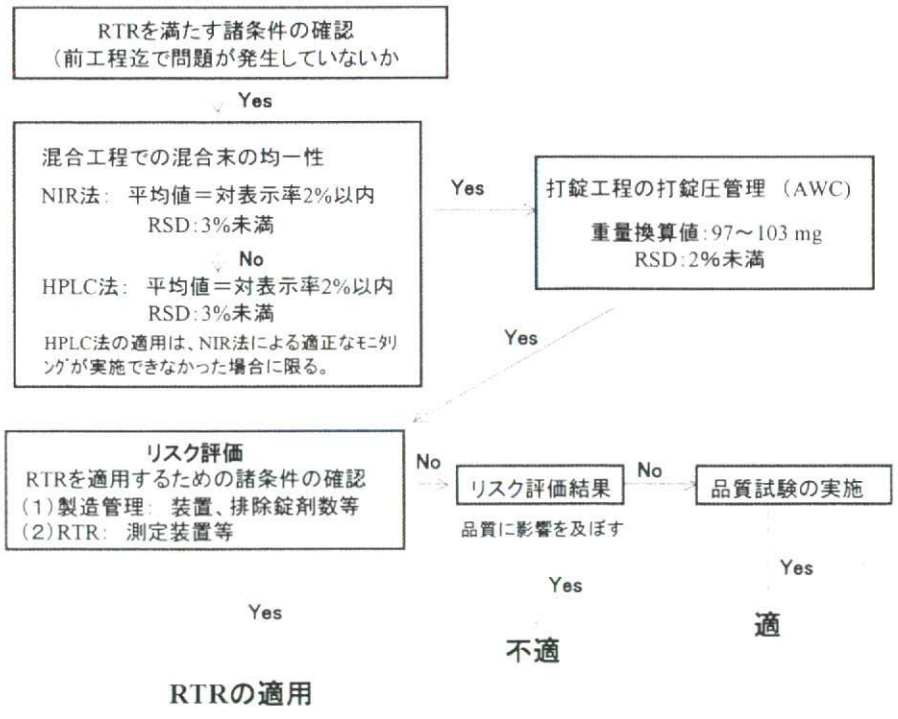

図 2（含量均一性の RTR 適用に至る手順）

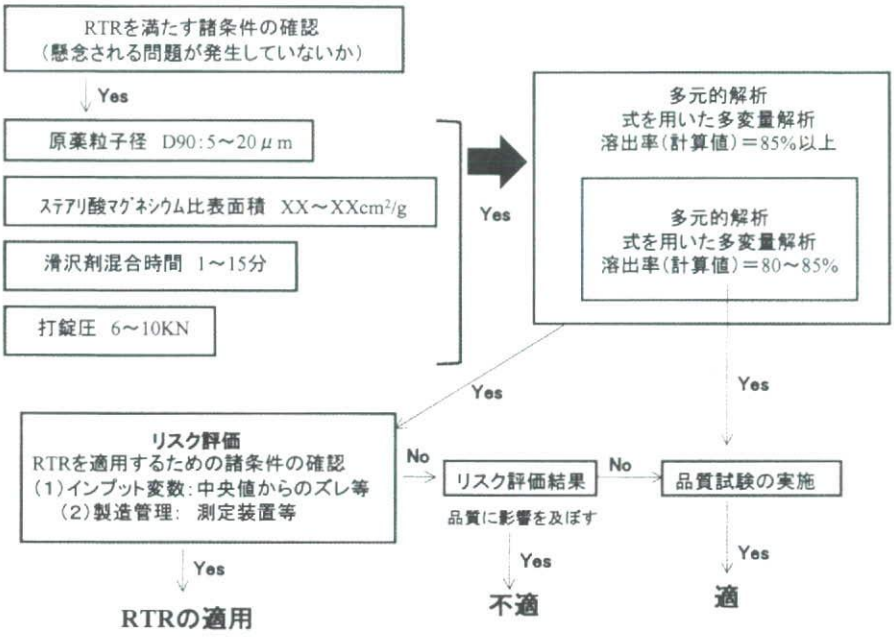

図 3（溶出性の RTR 適用に至る手順）

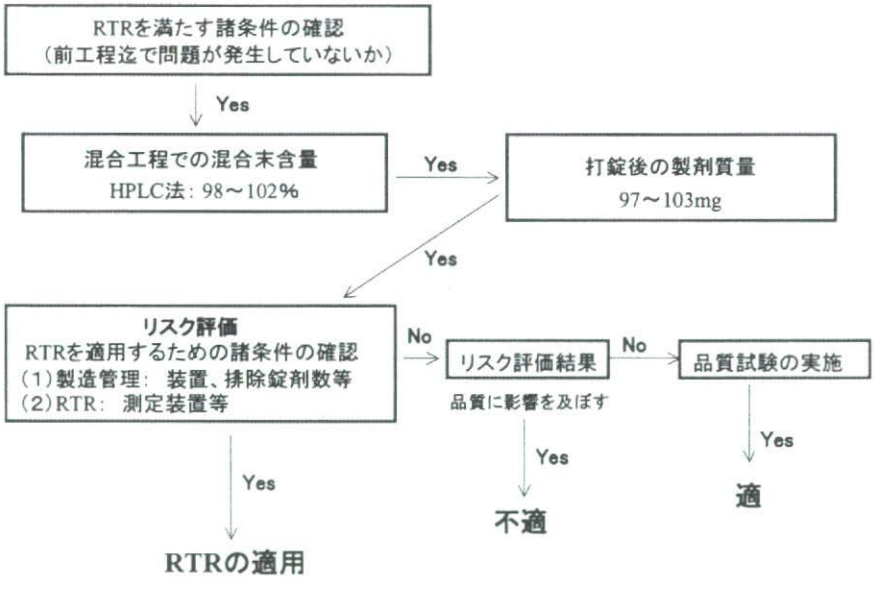

図 4（含量の RTR 適用に至る手順）

Application Form for Sakura Tablet

Mock-Up for the Manufacture Method, Specifications, and Test Method Columns of Drug Product (Sample Description)

Research on the construction of steady and efficient processes
for the manufacture, development, and approval review of drugs

First Section Meeting

[Manufacturing method]

[Scale of manufacturing process]:
Manufacture, packaging, labeling, storage, and testing of Sakura Tablet

Critical steps

<First Step> Blending process

<Second Step> Second blending process

<Third Step> Compression process

<First Step> Blending process
Blend <<30 w/w%>> amokinol, <<53 w/w%>> calcium hydrogen phosphate hydrate, <<10 w/w%>> D-mannitol, and <<5 w/w%>> sodium starch glycolate. Determine the blending endpoint according to [Process control 1]. [Process control 2]

<Second Step> Second blending process
To the mixture obtained from the First Step, add 2 w/w% magnesium stearate with respect to the composition of the Sakura Tablet, and blend the mixture using a tumbling mixer for <<1 to 15 min>>.

<Third Step> Compression process
Compress the mixture obtained from the Second Step at 6 - 10 kN using a rotary type tabletting machine (with a punch of 6 mm in diameter) [Process control 3]

<Fourth Step> Coating process
Transfer the compressed uncoated tablets that were manufactured in the Third Step into a coating pan, and spray coat them with a coating solution.

<Fifth Step> Packaging, labeling, and storage processes
Thereafter, fill "a polypropylene film"with the tablets that were already coated in the step mentioned above and package them into "aluminium foil" and seal it by heating with a blister packaging machine. Cut the sealed products to make PTP sheets and transfer them into "a carton box" and perform labeling appropriately. Store these labeled boxes and perform appropriate testing.

[Control item in the Second Step (Raw material)]
Specific surface area of magnesium stearate (Brunauer, Emmett, and Teller (BET) method)

[Process control 1]
Relative standard deviation: Less than 3% (near-infrared (NIR) method)

When the blend uniformity is tested according to the test method (NIR method) as determined under the uniformity of dosage units (RTRT) of [Specifications & test methods], the relative standard deviation is less than 3%.

[Process control 2]
Content: 98 to 102% (high-performance liquid chromatography (HPLC) method)

When the content is tested according to the test method (HPLC method) as observed in the assay (RTRT) of [Specifications & test methods], the content is equivalent to 98 to 102%.

[Process control 3]
When the mean weight of the tablet (following tablet compression) is measured, the content is 100 ± 3 mg.

[Specifications & test methods]

[Test name]: Content

[Specifications & test methods]
Sakura Tablet contains not less than 95.0 and not more than 105.0% of the labeled amount of amokinol ($C_{XX}H_{XX}N_XO_X$: XXX.XX).

[Specifications & test methods]

[Test name]: Description

[Specifications & test methods]
Sakura Tablet occurs as light red film-coated tablets.

[Specifications & test methods]

[Test name]: Identification

[Specifications & test methods]
Weigh XX g of powdered Sakura Tablet, equivalent to X mg of amokinol ($C_{XX}H_{XX}N_XO_X$). Add X mL of a mixture of acetonitrile and water (1:1), shake well for XX min, and filter. Discard the first 10 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, to X mg of amokinol reference standard add X mL of a mixture of acetonitrile and water (1:1), shake well for XX min, filter, and use the filtrate as the standard solution. Determine the absorption spectrum of the sample and standard solutions as directed under Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave number.

[Specifications & test methods]

[Test name]: Purity, related substances

[Specifications & test methods]
Weigh accurately not less than 20 tablets of Sakura Tablets and grind to powder. Weigh accurately a quantity of powdered Sakura Tablet, equivalent to X.XXX g of amokinol according to the labeled amount, add the mobile phase to make exactly XX mL, and use this solution as the sample solution. Separately, weigh accurately about X.XXX g of amokinol reference standard, dissolve in the mobile phase to make exactly XX mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample and standard solutions as directed under the Liquid Chromatography according to the following conditions. Determine the peak areas (A_T and A_S) of amokinol in the sample solution and the standard solution by the Automatic integration method: the amount of each related substance is not more than 0.2%, and the total amount of related substances is not more than 1.0%.

(Equation 1)

Operating conditions:

Detector:	An ultraviolet absorption photometer (wavelength, 210 nm)
Column:	A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).
Column temperature:	A constant temperature of about 40°C
Mobile phase:	A mixture of acetonitrile and water (1:1)
Flow rate:	Adjust the flow rate so that the retention time of amokinol is about X min.

System suitability:

Test for required detectability: Pipet 10 mL of the standard solution, and add the mobile phase to make exactly 100 mL. Confirm that the peak area of amokinol obtained from 20 μL of this solution is equivalent to 7% to 13% of that of the standard solution.

System performance: Dissolve X.XXX g each of amokinol and YYY in XX mL of the mobile phase. When the procedure is run with 20 μL of this solution under the above operating conditions, amokinol and YYY are eluted in this order with the resolution between the peaks being not less than XX.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions: the relative standard deviation of the peak area of amokinol is not more than 2.0%.

[Specifications & test methods]

[Test name]: Uniformity of dosage units (RTRT)

[Specifications & test methods]

This test is performed as a real-time release testing, which is subsequently to be established as the release specification.

The blend uniformity in the blending process <First Step> and the tablet weight in the compression process <Third Step> conform to the designated process control values.

Note: The blend uniformity in the blending process <First Step> is tested according to the following test method.

Perform the test as directed under Near-infrared Spectrophotometry (NIR) using the probe in diffuse reflection mode through a glass plate glass made of borosilicate glass from the outside of the operating blending equipment, and determine the blend uniformity according to the relative standard deviation of the assay values obtained at 6 consecutive points.

(Equation 2)

Operating conditions:

Measurement method: Diffuse reflectance

Light source: High-energy air-cooled NIR source

Detector: High-sensitive InGaAs detector

Scanning range: 7500 - 4000 cm^{-1}

Scanning frequency: 16-fold

Resolution: 8 cm^{-1}

Conditions for the pretreatment of spectrum: Multiplicative Scatter Correction (MSC)

Analytical method: Partial least squares (PLS)

System suitability:

System performance:

When the content is determined using the blending powder in which the content of the drug substance has been verified to be almost 100% according to a control evaluation procedure, the content is equivalent to 98.0% to 102.0% according to the labeled amount.

In this study, the following calibration and validation processes are performed; furthermore, a calibration curve obtained for the periodic revalidation implemented is used, where appropriate.

Calibration:

Use at least 5 samples of blending powder with different contents but with the same excipient rate as that of Sakura Tablet, which are prepared to contain drug substance in the range of 70% to 130% according to the labeled amount. Use MSC and PLS for the pretreatment of the spectrum and the analytical method respectively, to construct calibration curve.

Validation:

Validate the calibration curve obtained using the production lots that reflect the production on commercial-scale.

Periodic revalidation:

Validate the calibration curve using commercial-scaled production lots at appropriately predetermined intervals.

The control evaluation procedure to be used for the system suitability, calibration, and validation follows the Assay (RTRT) used in HPLC provided in the [Specifications & test methods] section.

[Specifications & test methods]

[Test name] Uniformity of dosage units

[Specifications & test methods]

This test can be substituted with the uniformity of dosage units (RTRT), which is a real-time release test, and is not performed at the time of release.

In case of any changes to the manufacturing process, perform the test according to the following method until the verification for each process control procedure is entirely completed: it meets the requirement of the Content uniformity test.

Furthermore, if the RTR is not applicable in a particular case in which no effect on the quality of Sakura Tablets has been verified in the results of risk assessment, perform the test according to the following method: it meets the requirement of the Content uniformity test. .

To 1 tablet of Sakura Tablet add 50 mL of a mixture of acetonitrile and water (1:1), and shake the mixture until the tablet is disintegrated. Expose the solution to ultrasonic vibration for 10 min, and add a mixture of acetonitrile and water (1:1) to make exactly 100 mL. Filter this solution through a membrane filter (pore size, 0.45 μm), and use the filtrate as the sample solution. Separately, weigh accurately about X.XX g of amokinol reference standard, and dissolve in a mixture of acetonitrile and water (1:1) to make exactly V mL. Pipet 5 mL of this solution, add a mixture of acetonitrile and water (1:1) to make exactly 100 mL, and use this solution as the standard solution. Perform the test with the sample and standard solutions as directed under Ultraviolet-visible Spectrophotometry, using a mixture of acetonitrile and water (1:1) as the control solution; determine the absorbance (A_T and A_S) of the sample solution and the standard solution at the wave length of 284 nm.

(Equation 3)

[Specifications & test methods]

[Test name]: Dissolution (RTRT)

[Specifications & test methods]

This test is performed as the real-time release testing, which is subsequently to be established as the release specification.

When the particle size of amokinol, specific surface area of magnesium stearate in the control of raw materials for the manufacture of Sakura Tablets [Magnesium stearate], blending time in the Second blending process <Second Step>, and the mean tablet compression force in the Compression process <Third Step> conform to the designated process control values, and when the dissolution rate calculated using the following equation is not less than 85%, it meets the requirements.

(Equation 4)

Note: The specific surface area of magnesium stearate is tested according to the following test method.

Specific surface area of magnesium stearate

Note) The details of the test method for evaluating specific surface area of magnesium stearate content have been provided below.

[Specifications & test methods]

[Test name]: Dissolution

[Specifications & test methods]

This test can be substituted with the Dissolution (RTRT) , which is a real-time release test, and is not performed at the time of release.

In cases of any changes to manufacturing process, perform the following dissolution test until the verification for each process control procedure is entirely completed. The value Q is specified to be 80%.

Furthermore, if the RTR method is not applicable in a particular case in which no effect on the quality of Sakura Tablets have not been verified in the risk assessment results, perform the following dissolution test. The value Q is specified to be 80%.

Perform the test with 1 tablet of Sakura Tablet using 900 mL of 0.1% sodium lauryl sulfate TS as the test solution according to paddle method at 50 rpm. Half an hour after the initiation of the test, filter not less than 20 mL of the dissolved solution through a membrane filter (pore size < 0.45 μm). Discard the first X mL of the filtrate, pipet the subsequent V mL, add 0.1% sodium lauryl sulfate TS to make exactly V′ mL, which contains XX μg of amokinol ($CXXHX_XN_XO_X$) per mL according to the labeled amount, and use this solution as the sample solution. Separately, weigh accurately about X.XX g of amokinol reference standard, and add XX mL of 0.1% sodium lauryl sulfate TS to make exactly XX mL. Pipet 1 mL of this solution, add 0.1% sodium lauryl sulfate TS to make exactly XX mL, and use this solution as the standard solution. Perform the test with the sample and standard solutions as directed under the Liquid Chromatography according to the following operating conditions. Determine the peak areas (A_T and A_S) of amokinol in the sample solution and the standard solution by the Automatic integration method.

(Equation 5)

Operating conditions:

Detector:	An ultraviolet absorption photometer (wavelength, 210 nm)
Column:	A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (particle diameter, 5 μm).
Column temperature:	A constant temperature of about 40°C
Mobile phase:	A mixture of acetonitrile and water (1:1)
Flow rate:	Adjust the flow rate so that the retention time of amokinol is about X min.
System suitability:	
System performance:	When the procedure is run with 20 μL of the standard solution under the above operating conditions, amokinol and internal standard substance are eluted in this order with the resolution between the peaks being not less than XX.
System repeatability:	When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions: the relative standard deviation of the peak area of amokinol is not more than 1.0%.

[Specifications & test methods]

[Test name]: Water

[Specifications & test methods]

Weigh accurately 10 tablets of Sakura Tablets and grind to powder. To powdered Sakura Tablets add 10 mL of methanol, shake well until it is disintegrated, and filter. Pipet 1 mL of the filtrate, and measure its water content as directed under Coulometric titration. Perform a blank determination, and make any necessary correction. The water content of the drug product is not more than 3%.

(Equation 6)

[Specifications & test methods]

[Test name]: Assay (RTRT)

[Specifications & test methods]

This test is performed as a real-time release test, which is subsequently to be established as the release specification.

The amount of amokinol is calculated using the following equation.

(Equation 7)

Note: The content of amokinol in the blended powder in the blending process is determined according to the following test method.

Weigh accurately XX mg of the blended powder, add exactly XX mL of the internal standard solution, and shake well for XX min. Centrifuge this solution, separate XX mL of the supernatant liquid, add the mobile phase to make XX mL, and use this solution as the sample solution. Separately, weigh accurately about X.XXX g of amokinol reference standard, and dissolve in the mobile phase to make exactly XX mL. To exactly XX mL of this solution, add the mobile phase to make XX mL, and use this solution as the standard. Perform the test with 20 μL each of the sample solution and the standard solution as directed under Liquid Chromatography according to the following conditions. Determine

the peak areas (Q_T and Q_S) of amokinol in the sample solution and the standard solution by the Automatic integration method.

(Equation 8)

Internal standard solution: A solution of benzophenone in a mixture of acetonitrile and water (1:1) (1 in 2000)

Operating conditions:

Detector:	An ultraviolet absorption photometer (wavelength, 210 nm)
Column:	A stainless steel column 4.6 mm in inside diameter of and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (particle diameter, 5 μm).
Column temperature:	A constant temperature of about 40°C
Mobile phase:	A mixture of acetonitrile and water (1:1)
Flow rate:	Adjust the flow rate so that the retention time of amokinol is about X min.
System suitability:	
System performance:	When the procedure is run with 20 μL of the standard solution under the above operating conditions, amokinol and internal standard substance are eluted in this order with the resolution between the peaks being not less than XX.
System repeatability:	When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions: the relative standard deviation of the peak area of amokinol is not more than 1.0%.

[Specifications & test methods]

[Test name]: Assay

[Specifications & test methods]

This test can be substituted with the Assay (RTRT), which is a real-time release test, and is not performed at the time of release.

In case of any changes to manufacturing process, the amount of amokinol is calculated according to the following assay method until the verification for each process control procedure is entirely completed.

Furthermore, if the RTR is not applicable in a particular case, in which no effect on the quality of Sakura Tablets have not been verified in the results of the risk assessment, the amount of amokinol is calculated according to the following assay method.

Weigh accurately not less than 20 Sakura Tablets and grind to powder . Weigh accurately a quantity equivalent to X.XXX g of amokinol according to the labeled amount, add exactly XX mL of the internal standard solution, and shake well for XX min. Centrifuge this solution, separate XX mL of the supernatant liquid, add the mobile phase to make XX mL, and use this solution as the sample solution.

Separately, weigh accurately about X.XXX g of amokinol reference standard, and dissolve in the mobile phase to make exactly XX mL. To exactly XX mL of this solution, add the mobile phase to make XX mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample and standard solutions as directed under Liquid Chromatography according to the following conditions. Determine the peak areas (Q_T and Q_S) of amokinol in the sample solution and the standard solution by the Automatic integration method.

(Equation 9)

Internal standard solution:	A solution of benzophenone in a mixture of acetonitrile and water (1:1) (1 in 2000)
Operating conditions:	
Detector:	An ultraviolet absorption photometer (wavelength, 210 nm)
Column:	A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).
Column temperature:	A constant temperature of about 40°C
Mobile phase:	A mixture of acetonitrile and water (1:1)
Flow rate:	Adjust the flow rate so that the retention time of amokinol is about X min.
System suitability:	
System performance:	When the procedure is run with 20 μL of the standard solution under the above operating conditions, amokinol and internal standard substance are eluted in this order with the resolution between peaks being not less than XX.
System repeatability:	When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions: the relative standard deviation of the peak area of amokinol is not more than 1.0%.

Application for Marketing Approval Attachment
(Proprietary name: Sakura Tablet 30 mg)

Equation 1 (Purity)

Amount of each related substance (mg) = $W_S \times A_T/A_S \times$ X.XXX

W_S: Amount (mg) of amokinol reference standard

Equation 2 (Uniformity of dosage units: RTRT)

Relative standard deviation (%) = X/s × 100

$$s = \sqrt{\sum_{i=1}^{n}(xi - \overline{X})^2 /(n-1)}$$

X: Mean of individual contents ($x_1, x_2, \cdot\cdot x_n$)

$x_1, x_2, \cdot\cdot x_n$: Individual contents of the dosage units tested.

n: Sample size (Total number of the samples tested)

s: Standard deviation of the sample

Equation 3 (Uniformity of dosage units)

Amount (mg) of amokinol = $W_S \times A_T/A_S \times$ X.XXX

W_S: Amount (mg) of amokinol reference standard

Equation 4 (Dissolution: RTRT)

Dissolution rate (%) with respect to the labeled amount of amokinol ($C_{XX}H_{XX}N_XO_X$)
= 108.9-11.96 × Particle size of amokinol [$\log_{10}$(d (0.9))]-7.556 × 10^{-5} × Specific surface area of magnesium stearate (cm^2/g) − 0.1849 × Lubricant blending time (min)-3.783 × 10^{-2} × Mean tablet compression force (N)

Equation 5 (Dissolution)

Dissolution rate (%) with respect to the labeled amount of amokinol ($C_{XX}H_{XX}N_XO_X$)
= $W_S \times A_T/A_S \times V'/V \times 1/C \times$ X.XXX

W_S: Amount (mg) of amokinol reference standard

C: Labeled amount (mg) of amokinol ($C_{XX}H_{XX}N_XO_X$) in 1 Sakura Tablet

Equation 6 (Water)

Water content (%) in amokinol
= [Water content (μg) in the sample - Water content (μg) in the blank determination solution] / Weight (mg) of 10 Sakura Tablets

Equation 7 (Assay: RTRT)

Content (%)of amokinol ($C_{XX}H_{XX}N_XO_X$) with respect to the labeled amount
=Content (%) of amokinol in the blended powder in the blending process <First Step>× Tablet weight (mg) following compression <Third Step> /C

C: Labeled amount (mg) of amokinol ($C_{XX}H_{XX}N_XO_X$) in 1 Sakura Tablet

Equation 8 (Assay: RTRT)

Amount (mg) of amokinol ($C_{XX}H_{XX}N_XO_X$) = $W_S \times Q_T/Q_S \times$ X.XXX

W_S: Amount (mg) of amokinol reference standard

Equation 9 (Assay)

Amount (mg) of amokinol ($C_{XX}H_{XX}N_XO_X$) = $W_S \times Q_T/Q_S \times$ X.XXX

W_S: Amount (mg) of amokinol reference standard

Attachment

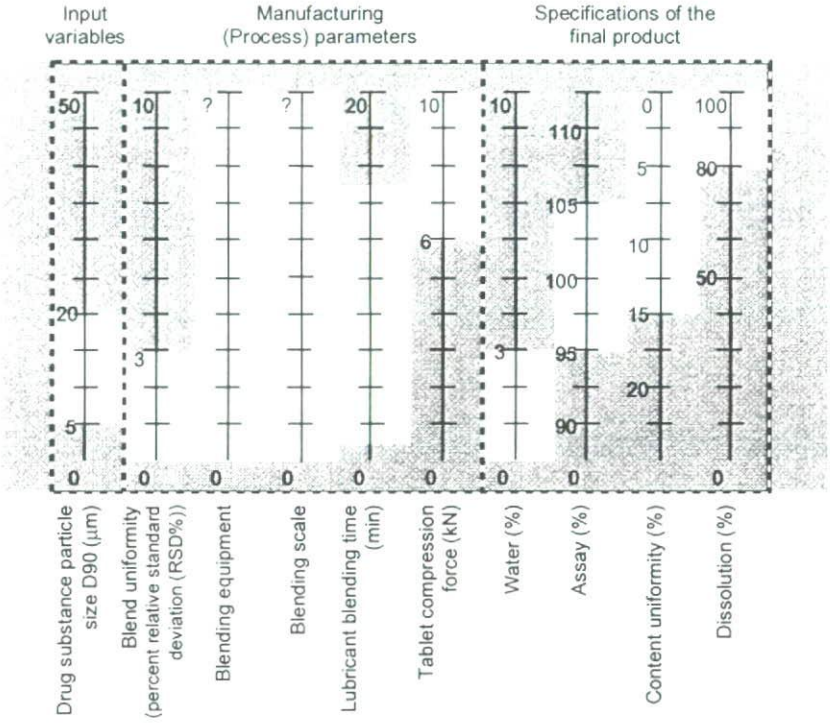

Figure 1 (Design Space and Specifications of Sakura Tablet 30 mg)

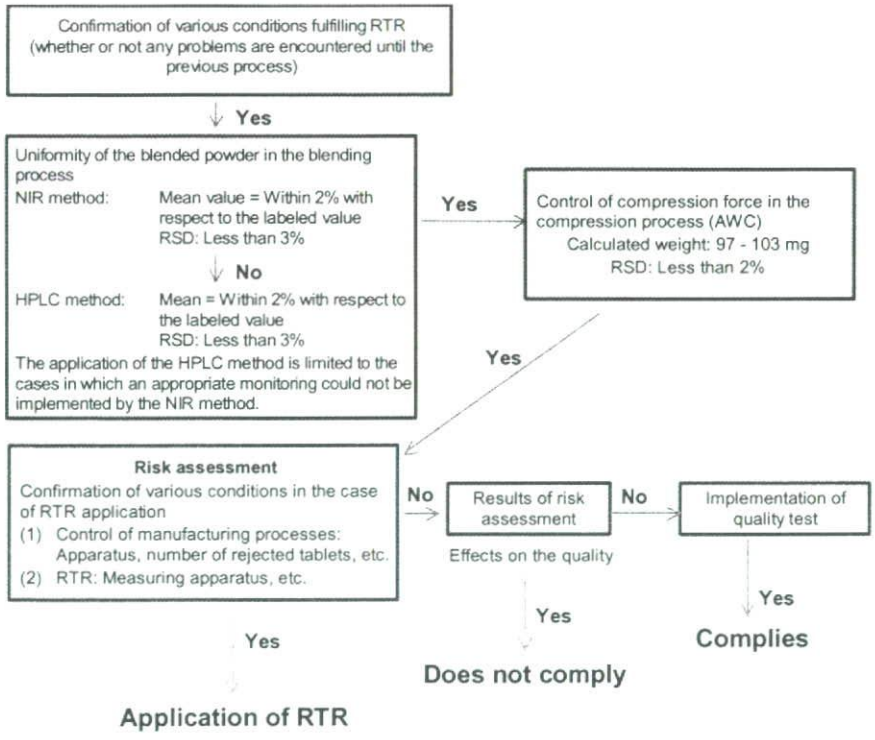

Figure 2 (Procedure for the Application of the RTR for Content Uniformity)

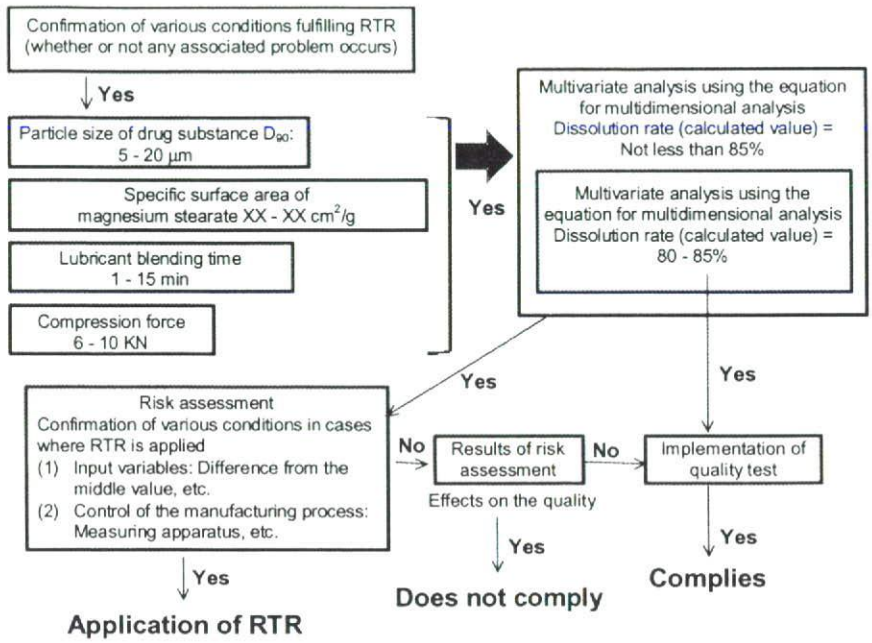

Figure 3 (Procedure for Applying the RTR to the Dissolution)

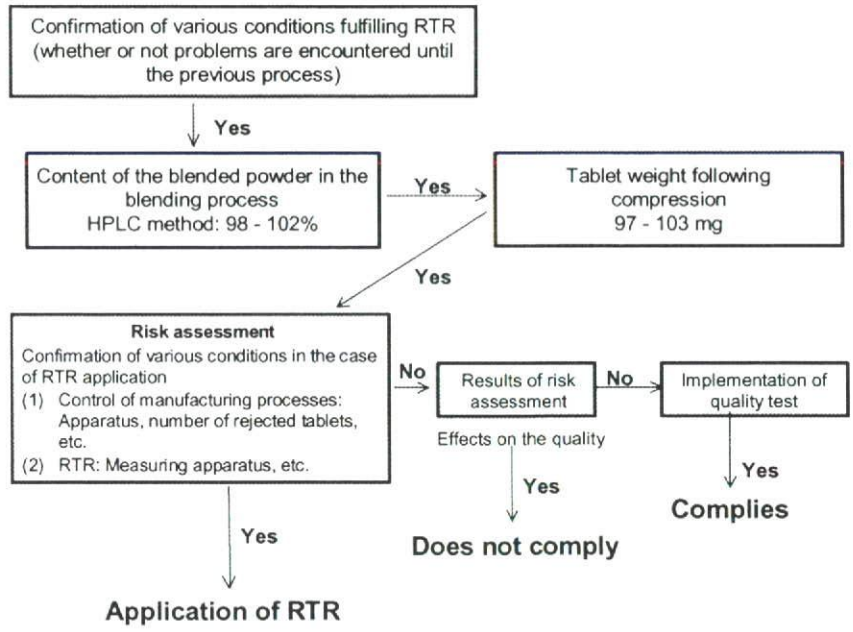

Figure 4 (Procedure for the Application of the RTR to the Content)

添付資料５

厚生労働科学研究
進捗報告／Q8関連

2008年4月21日 製薬協品質委員会

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はじめに

- ICH Q-trio（Q8・Q9・Q10）が作成される中、日本が昨年度実施してきた活動のレビュー
- 日本版Mock CTD作成の概要
- 今後の予定

ICH Q-trioの状況

- Q8
  - Q8：　Step 5（2006年9月1日）
  - Q8(R1)：　Step 3（2008年3月17日）
- Q9
  - Step 5（2006年9月1日）
- Q10
  - Step 3（2007年7月13日）

厚生労働科学研究の内容

- 医薬品製造開発・承認審査の確実かつ効率的なプロセス構築に関する研究
  - 主任研究員：　奥田先生
- 分科会
  - 第1分科会：　檜山先生
    - 重要工程におけるデザインスペース（DS）の設定及びControl StrategyとしてのReal Time Release等の研究
  - 第2分科会：　山田先生・奥田先生
    - 非重要の定義、非重要とした場合の製造法記載内容に関するBaseline Approach
  - 第3分科会：　四方田先生
    - 添加剤処方のDS研究

経緯： 研究班全体

- 立ち上げ： 2006年12月14日
- 2008年度（平成19年度）
  - 2007年8月9日： 第1回全体班会議
  - 2007年12月17日： 第2回
  - 2008年2月29日： 第3回（最終確認）

各分科会の状況（2月29日全体班会議から）

- 第1分科会： 後述
- 第2分科会
  - Baseline Approach ⇒ Minimal Approach / Q8(R1)
  - 重要工程の特定にQRMを検討*
- 第3分科会
  - 浸透圧を利用した放出制御システム（OROS）
  - コーティング基材の置換率の違いをコーティング量でコントロール ⇒ DS

*未確定

経緯： 第1分科会

- 2007年1月12日： サブグループ編成
  - DSサブグループ
  - 品質管理RTRサブグループ
- 2007年4月18日： AZよりたたき台提案
- 2007年7月28日： AZよりたたき台提示
- 2007年8月6日、9月10日、10月25日、11月20日、12月17日、2008年1月25日、2月20日： 修正

Mock CTDの位置付け

- Module 2のMock（Q8 = Module 3）： QOS
  - Module 3のボリューム
  - 日本の審査ではModule 2中心
- 以下の基礎情報はModule 3に記載する事項として成果物の別添資料とする。
  - リスク評価、製造工程の詳細やバリデーション、リアルタイムリリース