

# Study Protocol

## MX137575

### Phase III Clinical Trial

Study of the Drug's Action in Long-Term Dosing on Depression and Depressive Conditions in the Field of Psychosomatic Medicine

#### Synopsis of study protocol

(1) Classification	Phase III clinical trial (long-term administration)
(2) Objectives	To study the safety as well as the efficacy and usefulness of MX137575 in long-term administration on depression and depressive conditions in psychosomatic medicine patients in a multicenter collaborative study, using the overall safety rating, final global improvement rating and usefulness as the main evaluation items. In addition, as secondary objectives, to study the weekly global severity rating and global improvement rating, the Hamilton Depression Rating Scale (HAMD), the changes over time in the physical / psychiatric symptoms, the global usefulness rating (4th week) and the adverse drug reactions (including abnormal laboratory test results and physiological test results) by individual.
(3) Subjects	Depression, depressive conditions Patients satisfying the following standards will be selected. (1) DSM-IV classifications of Major depression, single episode (296.21 – 296.24) Major depression, recurrent (296.31 – 296.34) Dysthymic disorder (300.4) Depressive disorder, not otherwise specified (311) Adjustment disorder with depressed mood (309.0)  (2) 20 to 69 years old (on date of consent), regardless of sex and inpatient/outpatient status

(4) Study method	Non-blind multicenter collaborative study using the single-group fixed-flexible method of administration
(5) Administration method Dose Dosing period	Fixed-flexible method of administration Single daily oral administration after breakfast Initial dose of 5 or 10 mg/day, maximum dose of 30 mg/day 26-52 weeks (regardless of interruptions of the treatment during the study period)
(6) Main endpoints	Final global improvement rating, overall safety rating, usefulness
(7) Secondary endpoints	Global severity rating, global improvement rating, HAMD, physical / psychiatric symptoms, global usefulness rating (4 <sup>th</sup> week), adverse drug reactions, laboratory test results, physiological test results
(8) Target number of study subjects	100 study subjects
(9) Study period	September 1997 – March 2001

**This study will be conducted in accordance with the trial protocol and in compliance with the "Guidelines for Good Clinical Practice for Trials on Pharmaceutical Products (GCP)," which have been established on the basis of the provisions of Articles 14-3 and 80-2 of the Pharmaceutical Affairs Law.**

1. Course of development

MX137575 is a newly screened non-tricyclic antidepressant that has been synthesized by XXXX & Co. (U.S.) The drug was shown, in vitro and in vivo, to potentially inhibit the reuptake of both serotonin and norepinephrine, and its effect was demonstrated in various depression models. On the other hand, the drug has low affinity to the receptors of various neurotransmitters and is thought to have few adverse drug reactions related to anticholinergic action,  $\alpha_1$ -blocking action, etc.

In phase I studies, the drug was tested in single doses given to healthy adult males (10 mg, 20 mg, 40 mg once a day), followed by a study on the effects of meals on its action and a repeated dose study (20 mg, 40 mg, once a day for 7 days). These trials confirmed the favorable absorption and tolerance of the drug, and moved on to phase II studies examining depression and depressive conditions.

Phase II open studies were conducted in psychiatric departments (2 studies) and a psychosomatic medicine department. In the psychiatric departments (dose: 10-30 mg/day, dosing period 6 weeks), the rates of improvement (substantial improvement + improvement) of the final global improvement rating were 52.2% (36/69) and 53.5% (23/43), and in the psychosomatic medicine department (dose: 5-20 mg/day, dosing period 4 weeks) the improvement rate was 63.8% (44/69). Adverse drug reactions included "constipation", "dry mouth", "nausea / vomiting", "drowsiness", "loss of appetite", etc., but none of them was serious (incidence: psychiatric departments: 38.7% (29/75) and 34.0% (16/47), psychosomatic medicine department: 27.3% (21/77)). No marked deterioration caused by the drug was seen in the laboratory test results.

Next, in order to determine the optimum dose range in phase III studies of the drug as an antidepressant, a double-blind intergroup comparative study (late phase II study) was conducted in psychiatric departments using imipramine hydrochloride as a control (June 1994 – January 1996). The subjects of the study had depression and depressive conditions and the doses were set at 50-150 mg of imipramine hydrochloride and 10-30 mg of MX137575. The results showed that the improvement rate (substantial improvement + improvement) of the final global improvement rating was 60.2% (41/68) for imipramine hydrochloride vs. 60.5% (49/81) for MX137575, and no significant difference was found between the two drugs. The safety rate (proportion of cases in which the drug was determined "safe") with respect to the overall safety rating was 26.9% (21/78) for imipramine hydrochloride vs. 42.9% (36/84) for MX137575, and the safety rate of MX137575 was significantly higher ( $p = 0.0478$ ).

Comparing the adverse drug reactions, we note that the incidence of adverse drug reactions tended to be lower for MX137575 than for imipramine hydrochloride, and the incidences of anticholinergic adverse drug reactions (especially dry mouth) and circulatory system adverse drug reactions were significantly lower for

MX137575 than for imipramine hydrochloride. In studying the usefulness, the usefulness rate (proportion of cases determined “rather useful” or higher) was 51.3% (40/78) for imipramine hydrochloride vs. 56.0% (47/84) for MX137575, and no significant difference was found. Nevertheless, the results of a similarity test, conducted using the handicap formula, demonstrated similarity of both drugs (the usefulness of MX137575 was not inferior to that of imipramine hydrochloride by 10% or more) in terms of their usefulness.

Based on the above, it appeared that MX137575 could be expected to have the same usefulness as imipramine hydrochloride at 1/5 its dose and that its optimum dose range is would be 10-30 mg.

Based on the above findings and because MX137575 is expected to be administered for extended periods, it was decided to study its safety as well as the efficacy and usefulness in the treatment of depression and depressive conditions in long-term administration to patients under psychiatric or psychosomatic medical care. This study protocol concerns the study on psychosomatic medicine patients.

2. Study objectives

To study the safety as well as the efficacy and usefulness of MX137575 in long-term administration on depression and depressive conditions in psychosomatic medicine patients in a multicenter collaborative study, using the overall safety rating, final global improvement rating and usefulness as the main evaluation items. In addition, as secondary objectives, to study the weekly global severity rating and global improvement rating, the Hamilton Depression Rating Scale (HAMD), the changes over time in the physical / psychiatric symptoms, the global usefulness rating (4th week) and the adverse drug reactions (including abnormal laboratory test results and physiological test results) by individual.

3. Standards for selection, exclusion and discontinuation of study subjects

Patients who meet all of the following standards and who, prior to the study, fully understand the objectives and descriptions of the study drug and the study and give their written consent, signed by the study subject or their legally acceptable representative (a person authorized to give their consent in place of the study subject), will be enrolled as study subjects.

**3-1. Target diseases**

Depression, depressive conditions

Patients who meet the following standards will be selected.

DSM-IV classifications of:

Major depression, single episode	(296.21 – 296.24)
Major depression, recurrent	(296.31 – 296.34)
Dysthymic disorder	(300.4)
Depressive disorder, not otherwise specified	(311)
Adjustment disorder with depressed mood	(309.0)

### **3-2. Selection standards**

- (1) Age: 20 to 69 years old (on date of consent)
- (2) Sex: Irrelevant
- (3) Inpatient/outpatient status: Irrelevant  
If the inpatient/outpatient status does change after the beginning of dosing, the date of change and the reason will be documented in the case records.

#### **Rationale for determination**

- (1) was established in accordance with the phase II study.
- (3) was established because a change in the environment may have an effect on the symptoms.

### **3-3. Exclusion standards**

Patients who satisfy the following standards will be excluded:

- (1) Patients with schizophrenia or convulsive disorders such as epilepsy or patients with a history of these disorders.
- (2) Patients with serious organic encephalopathy
- (3) Patients with suicidal tendencies for whom the course of the study may be difficult (4 points in the HAMD (Suicide Item) score)
- (4) Patients with acute narrow-angle glaucoma, dysuria or increased intraocular pressure
- (5) Patients with a serious\* hormonal dysfunction such as hypothyroidism
- (6) Patients with a serious\* cardiac, hepatic or renal dysfunction and patients with a hematopoietic disorder
- (7) Patients with a drug allergy or with a history of drug allergy
- (8) Patients with urinary stasis caused by prostatic hypertrophy
- (9) Patients who took an MAO inhibitor 2 or fewer weeks before receiving the study drug
- (10) Patients who took a lithium drug 2 or fewer weeks before receiving the study drug
- (11) Patients who are pregnant or may be pregnant and breastfeeding patients
- (12) Patients who received a different study drug within the past 3 months
- (13) Patients deemed ineligible by the chief investigator or an investigator for other reasons.

(Note) \* See "Standards for classification of the severity of adverse drug reactions of medicinal agents" (Drug Safety (80), June 29, 1992)

#### **Rationale for determination**

- (1) will be excluded because of the danger of aggravating the positive symptoms of schizophrenia. Patients with epilepsy were excluded because of the risk of inducing an epileptic attack.
- (2), (9) and (10) will be excluded because of difficulty in evaluating the efficacy of MX137575.
- (3) will be excluded out of ethical considerations concerning the study subjects.

(4) will be excluded because of the danger of aggravating their symptoms through the anticholinergic action of the drug.

(5) will be excluded because of difficulty in evaluating the efficacy of the drug.

(6)-(8) will be excluded because of ethical considerations and because of difficulty in evaluating the drug's safety.

(11)-(13) will be excluded out of concern for the study subjects' safety.

### **3-4. Standards for discontinuation of treatment**

In cases in which the study is interrupted because of the following reasons, the study subjects will be regarded as discontinued cases, the chief investigator or an investigator will decide on a suitable treatment and the reason for discontinuation and the date of discontinuation will be recorded in the case records. In case several reasons were applicable, all the applicable items will be marked with ○ and one of them, considered the primary reason, will be marked with ⊙. In principal, the necessary items will be examined and evaluated upon a subject's discontinuation. If a study subject stops coming to the hospital, follow-up observations will be conducted, whenever possible, and the reason they stopped coming to the hospital and the ensuing course will be surveyed and documented. However, the privacy of the study subject will be fully respected as regards the characteristics of their disease. Moreover, no new study subjects will be enrolled to replace the discontinued study subjects.

- (1) Cases in which the symptoms worsened because the effect of the drug was insufficient or cases in which the effectiveness of the drug is deemed undetectable
- (2) Cases in which continuation of treatment is deemed difficult because of the appearance of adverse drug reactions, because of the appearance of new symptoms, etc.
- (3) Cases in which the study subject or their representative indicate that they wish to withdraw from the study
- (4) Cases of pregnancy or suspected pregnancy during the treatment
- (5) Others, study subjects deemed ineligible by the chief investigator or an investigator.

### **Rationale for determination**

(1), (2), (4) and (5) were established out of safety considerations.

(3) is an explanatory item for obtaining the consent of the study subject.

#### **4. Consent of study subjects**

Prior to the study, the chief investigator will prepare a consent form in collaboration with the study sponsor and obtain the approval of the Institutional Review Board. The chief investigator or an investigator will explain the following items, determined in GCP, using the approved explanatory document, confirm that the study subject fully comprehends its description and obtain their consent, voluntarily given, to be a study subject, before recording the "Study Subject's Correspondence Card."

In case of doubt about the power of discernment of the patient, the consent will be obtained from their representative (a person authorized to give their consent in place of the study subject), and the reason for it will be documented in the case records.

The subject's consent will be indicated in writing and the date of consent and the name of the person who gave the consent (in the case of a representative, their relationship with the study subject) will be recorded in the appropriate column in the case records.

In addition, in case a consent concerning measurement of the plasma concentration of the drug (unchanged substance) is also obtained, the study subject's own signature will be obtained in the appropriate column in the consent form and the instruction will be recorded in the case records. This will not be possible if the consent is given by a representative.

#### Explanatory items

- (1) The fact that the study is related to research
- (2) The study objectives
- (3) The study method
- (4) Expected duration of the participation of the study subject in the study
- (5) Target number of study subjects in the study
- (6) Anticipated clinical benefits and foreseeable risks or inconveniences
- (7) Alternative courses of therapy for the disease that may be available and their important potential benefits and risks
- (8) Compensation and treatment the study subject will be entitled to in case of health impairment related to the study
- (9) That the study subject voluntarily agrees to participate in the study and that the study subject or their representative will be able to refuse to participate or withdraw from the study at any time. In addition, that the study subject will not incur any penalty or loss of benefits to which they are otherwise entitled because of such a refusal or withdrawal.
- (10) That if any information becomes available that may be relevant to the willingness of the study subject or their representative to continue participation in the study, it will be communicated in a timely manner to the study subject or their representative.
- (11) The conditions or reasons for discontinuing the participation of the study subject in the study.
- (12) That the monitor, auditor, Institutional Review Board and regulatory authorities will be allowed to review the source medical records. That in such a case the identity of the study subject will remain confidential. That by signing the consent form, the study subject or their representative approves such a review.
- (13) That even if the results of the study are published, the identity of the study subject will remain confidential.
- (14) Expenses incurred by the study subject.
- (15) Surname, official title and contact information of the chief investigator or investigator.

(16) The liaison at the medical institution who can answer inquiries or be contacted for further information regarding the study and the study subjects' rights or in the event of study-related health impairment.

(17) Regulations the study subject has to observe.

In addition, the chief investigator or an investigator will check with the study subject if there are other attending physicians, and upon receiving the consent of the study subject will inform the other attending physicians of the participation of the study subject in the study.

# 治験実施計画書

## MX137575

### 第Ⅲ相臨床試験

—精神科領域におけるうつ病，うつ状態に対する長期投与試験—

#### 治験実施計画の要約

(1) 区 分	第Ⅲ相臨床試験（長期投与試験）
(2) 目 的	多施設共同治験により，精神科領域でのうつ病，うつ状態に対するMX137575の長期投与時における安全性，さらに有効性及び有用性を，概括安全度，最終全般改善度，有用度を主要評価項目として検討する。さらに副次的に，週別に評価される全般重症度，全般改善度，Hamiltonのうつ病評価尺度（HAM-D），全般有用度（4週目），症例毎に評価される副作用（臨床検査，生理学的検査異常変動を含む）を検討する。
(3) 対 象	うつ病，うつ状態 下記の基準に該当する患者を選択する。 ①DSM-IV分類の 大うつ病性障害，単一エピソード (296. 21～296. 24) 大うつ病性障害，反復性 (296. 31～296. 34) 気分変調性障害 (300. 4) 双極Ⅰ型障害，最も新しいエピソードがうつ病 (296. 51～296. 54) 双極Ⅱ型障害（軽躁病エピソードを伴う反復性大うつ病エピソード） (296. 89) ②年齢は20歳以上70歳未満（同意取得日）とし，性別および入院・外来は問わない。
(4) 試 験 方 法	単一群のFixed-flexible投与方法による非盲検の多施設共同治験

<p>(5) 投与方法          投与量          投与期間</p>	<p>Fixed-flexible投与方法          1日1回朝食後に経口投与する。          初期用量 10mg/日, 最高用量 40mg/日          26～52週間 (ただし途中の服薬中断が何回あっても構わない)</p>
<p>(6) 主要評価項目</p>	<p>最終全般改善度, 概括安全度, 有用度</p>
<p>(7) 副次的評価項目</p>	<p>全般重症度, 全般改善度, HAM-D,          全般有用度(4週目), 副作用, 臨床検査値, 生理学的検査値</p>
<p>(8) 目標症例数</p>	<p>300例</p>
<p>(9) 治験実施期間</p>	<p>1997年12月～2001年3月</p>

本治験は薬事法第14条第3項および第80条の2の規定にもとづいて定められた「医薬品の臨床試験の実施に関する省令」（GCP）および本治験実施計画書を遵守して実施する。

## 1. 開発の経緯

MX137575は米国イーライリリー社で合成、スクリーニングされた新規の非三環系抗うつ薬である。本薬は *in vitro* および *in vivo* でセロトニンおよびノルエピネフリンの再取り込みを共に強く阻害し、種々のうつ病モデルで効果を示すことが証明されている。一方、本薬は、種々の神経伝達物質受容体に対する親和性は弱く、抗コリン作用、 $\alpha_1$ 遮断作用等に基づく副作用は少ないと考えられる。

本薬の第Ⅰ相試験は健常成人男子を対象に単回投与試験（1日1回10mg, 20mg, 40mg）を実施し、引き続き、食事の影響試験、反復投与試験（1日1回20mg, 40mg, 7日間）を実施した。これらの試験において、薬物の吸収性は良好であり、本薬の忍容性が確認されたため、うつ病、うつ状態を対象とした第Ⅱ相試験に移行した。

第Ⅱ相オープン試験は精神科（2試験）と心療内科で実施した。精神科（投与量：10～30mg/日、投与期間：6週間）での最終全般改善度の改善（著明改善+改善）率は52.2%（36/69）、53.5%（23/43）であり、心療内科（投与量：5～20mg/日、投与期間：4週間）での改善率は63.8%（44/69）であった。副作用としては、「便秘」、「口渇」、「悪心・嘔吐」、「眠気」、「食欲不振」などが認められたが、重篤なものはなかった（発現頻度：精神科38.7%（29/75）、34.0%（16/47）、心療内科27.3%（21/77））。また、臨床検査値については、薬剤に起因して著しく悪化したものは認められなかった。

次に本薬の抗うつ薬として第Ⅲ相試験で用いる至適用量幅を設定する目的で、精神科において、塩酸イミプラミンを対照薬として二重盲検群間比較試験（後期第Ⅱ相試験）を実施した（1994年6月～1996年1月）。対象はうつ病、うつ状態、投与量は塩酸イミプラミンが50mg～150mg、MX137575が10mg～30mgまでと設定した。この結果、塩酸イミプラミンの最終全般改善度の改善（著明改善+改善）率は60.3%（41/68）であるのに対し、MX137575は60.5%（49/81）であり、両薬剤間に有意差は認められなかった。概括安全度について安全率（「安全である」と判定された症例の占める割合）は塩酸イミプラミンが26.9%（21/78）、MX137575が44.0%（37/84）であり、MX137575の安全率が有意に高かった（ $p=0.0478$ ）。

副作用を比較した場合、発現件数で本薬は塩酸イミプラミンに比して少ない傾向を示し、抗コリン系の副作用（特に口渇）および循環器系の副作用は塩酸イミプラミンに比して有意に少なかった。また有用度について、塩酸イミプラミンの有用率（「かなり有用」以上の症例の占める割合）は51.3%（40/78）であるのに対し、

MX137575が56.0%（47/84）であり、有意差は認められなかった。しかしながら、ハンディキャップ方式による同等性検証の結果から有用率について両薬剤の同等性（

MX137575の有用率は塩酸イミプラミンより10%以上劣らないこと）が立証された。

以上よりMX137575は塩酸イミプラミンの1/5の用量で同等の有用性が期待でき、至適用量幅は10～30mgと考えられた。

以上の経緯に基づき、本薬が長期間にわたる投与が想定されることから、精神科領域および心療内科・内科領域におけるうつ病、うつ状態に対する長期投与時

の安全性, さらに有効性, 有用性を検討することとした。本治験実施計画は精神科領域における検討を行うものである。

## 2. 治験の目的

多施設共同治験により、精神科領域でのうつ病、うつ状態に対するMX137575の長期投与時における安全性、さらに有効性及び有用性を、概括安全度、最終全般改善度、有用度を主要評価項目として検討する。さらに副次的に、週別に評価される全般重症度、全般改善度、Hamiltonのうつ病評価尺度（HAM-D）、全般有用度（4週目）、症例毎に評価される副作用（臨床検査、生理学的検査異常変動を含む）を検討する。

## 3. 被験者の選択、除外、中止基準

以下の基準を満たし、さらに治験に先立ち治験薬および治験の目的、内容につき十分な説明を行った後に被験者または代諾者（被験者に代わって同意を成し得る者）より文書同意の得られた患者を対象とする。

### 3-1. 対象疾患

うつ病、うつ状態

下記の基準に該当する患者を選択する。

DSM-IV分類の

大うつ病性障害、単一エピソード	(296. 21 ~ 296. 24)
大うつ病性障害、反復性	(296. 31 ~ 296. 34)
気分変調性障害	(300. 4)
双極Ⅰ型障害、最も新しいエピソードがうつ病	(296. 51 ~ 296. 54)
双極Ⅱ型障害（軽躁病エピソードを伴う反復性大うつ病エピソード）	(296. 89)

なお、「ICD-10」の病型分類を併記する。

### 3-2. 選択基準

- ①年齢：20歳以上70歳未満（同意取得日）
- ②性別：不問
- ③入院・外来：不問

ただし、投与開始後に入院・外来の変更を行った場合は変更日および理由を症例報告書に記載する。

[設定の根拠]

- ①は、第Ⅱ相試験に合わせて設定した。
- ③は、環境の変化が症状に影響を与えるおそれがあるため設定した。

### 3-3. 除外基準

以下に該当する患者は除外する。

- ①精神分裂病およびてんかん等のけいれん性疾患またはこれらの既往を有する患者
- ②器質的脳障害の患者
- 3 治験の進行が困難と考えられる自殺傾向の著しい患者（HAM-D（自殺の項目）のスコアが4点）
- ④現在治療中の甲状腺機能低下症等のホルモン機能異常のある患者

- 5 現在治療中の心，肝，腎機能障害のある患者および造血器障害のある患者
- ⑥ 薬物アレルギーの患者，あるいはその既往のある患者
- ⑦ MAO阻害薬を本薬投与前2週間以内に服用した患者
- ⑧ リチウム薬を本薬投与前2週間以内に服用した患者
- ⑨ 妊婦もしくは妊娠している可能性のある患者，および授乳中の患者
- ⑩ 過去3ヶ月以内に他の治験薬を投与された患者
- 11 その他，治験責任医師または治験分担医師が不適当と判断した患者

なお，急性狭〔隅〕角緑内障・眼内圧亢進等のある患者，排尿困難・前立腺肥大症による尿うっ滞のある患者に投与する場合は，これらの症状の変化に十分注意しながら慎重に投与する。

〔設定の根拠〕

- 1 は，精神分裂病の陽性症状が悪化するおそれがあるため除外とした。てんかんを有する症例は発作を惹起するおそれがあることから除外とした。
- 2，⑦，⑧は，本薬の薬効評価が困難なため除外とした。
- ③は，被験者に対する倫理的側面より除外とした。
- ④は，薬効評価が困難なため除外とした。
- ⑤，⑥は，倫理的側面および安全性の評価が困難なため除外とした。
- ⑨～⑪は，被験者に対する安全性を考慮して除外とした。

3-4. 投与中止基準

下記理由等によって治験が打ち切られた場合，その患者を中止例とし，治験責任医師または治験分担医師は適切な処置を行うとともに，中止の理由およびその年月日を症例報告書に記載する。ただし，複数の理由が考えられる場合には該当する項目全てに○を付し，その中で主な理由と考えられるもの1つに◎を付す。中止した症例については原則としてその時点で必要な項目を観察し評価を行う。また，患者が来院しなくなった場合，可能な限り追跡調査を行い，来院しなくなった理由，その後の経過等について調査し，記載する。ただし，疾患の特質上患者のプライバシーには十分配慮すること。なお，中止した症例に代わる症例として新たな症例の登録は行わない。

- ① 本薬の効果が不十分で症状の悪化または本薬の有効性が認められないと判断される場合
- ② 副作用の発現等により本薬の投与継続が困難であると判断される場合
- ③ 患者もしくは代諾者より治験からの離脱の申し入れがある場合
- ④ 本薬投与中に妊娠あるいは妊娠の疑いが生じた場合
- ⑤ その他，治験責任医師または治験分担医師が投与継続が困難であると判断した場合

〔設定の根拠〕

- ①，②，④，⑤は安全性配慮のため，設定した。
- ③は被験者との同意取得時の説明事項である。

#### 4. 被験者の同意

治験の実施に先立ち、治験責任医師は、治験依頼者の協力を得て説明文書を作成し、治験審査委員会で承認を得る。治験責任医師または治験分担医師は、承認された説明文書を用いて、GCPで定める下記の事項について説明し、患者が内容を十分理解したことを確認した上で、被験者になることについての本人の自由意思による同意を「症例連絡票」記載前に得る。

判断能力に疑問が持たれるような場合には代諾者（被験者に代わって同意を成し得る者）による同意を得ることとし、その理由を症例報告書に記載する。

同意は文書によるものとし、同意年月日、同意者（代諾者の場合は被験者との続柄）を症例報告書の該当欄に記載する。

##### 「説明事項」

- (1) 治験が研究を伴うこと
- (2) 治験の目的
- (3) 治験の方法
- (4) 被験者の治験への参加予定期間
- (5) 治験に参加する予定の被験者数
- (6) 予期される臨床上の利益および危険性または不便
- (7) 当該疾患に対する他の治療方法の有無および予測される重要な利益および危険性
- (8) 治験に関連する健康被害が発生した場合に被験者が受けることのできる補償および治療
- (9) 治験への参加は被験者の自由意思によるものであり、被験者またはその代諾者は被験者の治験への参加を随時拒否または撤回できること。また、拒否・撤回によって被験者が不利な扱いを受けたり、本来受けるべき利益を失うことがないこと。
- (10) 治験への参加の継続について被験者またはその代諾者の意思に影響を与える可能性のある情報が得られた場合には速やかに被験者またはその代諾者に伝えられること。
- (11) 治験への参加を中止させる場合の条件または理由
- (12) モニター、監査担当者、治験審査委員会および規制当局が原医療記録を閲覧できること。その際、被験者の秘密は保全されること。また、同意文書に被験者または代諾者が署名することによって閲覧を認めたことになること。
- (13) 治験の結果が公表される場合であっても、被験者の秘密は保全されること。
- (14) 被験者の費用負担
- (15) 治験責任医師または治験分担医師の氏名、職名、および連絡先
- (16) 被験者が治験および被験者の権利に関してさらに情報が欲しい場合、または治験に関連する健康被害が生じた場合に照会すべきまたは連絡を取るべき医療機関の相談窓口
- (17) 被験者が守るべき事項

なお、治験責任医師または治験分担医師は被験者に他の主治医がいるか否かを確認し、被験者の同意のもとに、主治医に被験者の治験への参加について連絡する。