INTERNATIONAL FEDERATION
OF FERTILITY SOCIETIES

# IFFS Surveillance 2013



October 2013

The International Federation of Fertility Societies (IFFS) is a federation of national membership societies that have an interest in the clinical and research aspects of reproduction and fertility. IFFS is a Non-Governmental Organization (NGO) in official relations with the World Health Organization (WHO).

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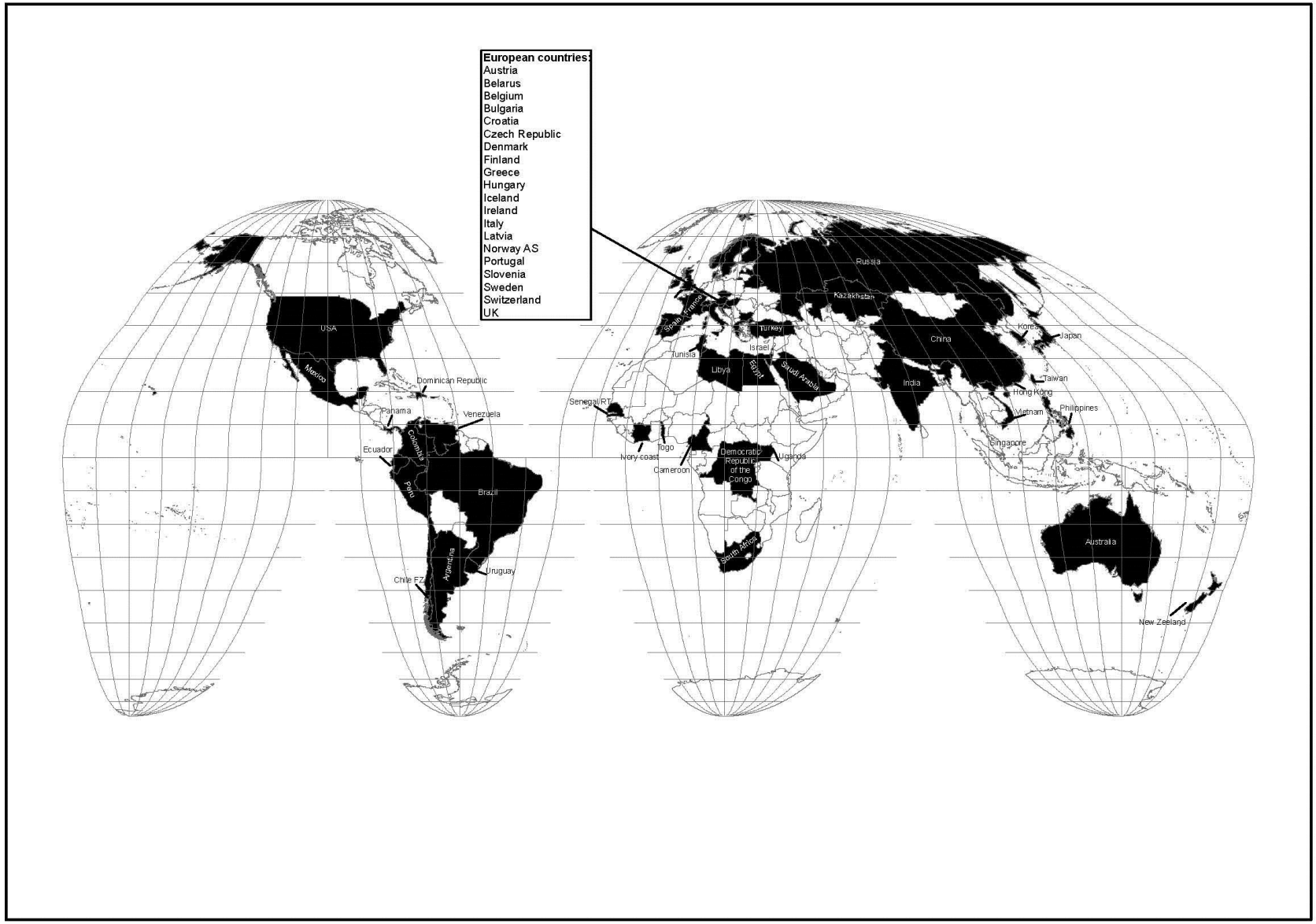
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Surveillance 2013 Dedication

The 2013 edition of Surveillance is dedicated to Dr. David Healy, late IFFS president, whose premature loss made this edition of Surveillance particularly challenging. Professor Healy made substantial academic, inspirational, executive, and financial contributions to this project at the outset, and we profoundly regret that he was not able to see the final product that he had so passionately championed.

## List of Participants (Survey Respondents)

| Country; of origin for the National Fertility Society - Member of IFFS or the equivalent | Respondent: Representing the professional National Fertility Society members or Fertility specialist |
|---|---|
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| Argentina | Ester Polak de Fried |
| Austria | Wilfried Feichtinger |
| Australia | Ossie Petrucco |
| Australia | Elizabeth Sullivan |
| Belarus | Oleg Tishkevich |
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| Colombia | Guido Parra |
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| Finland | A. Tiitinen |
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**List of Participants (continued)**

| Country; of origin for the National Fertility Society - Member of IFFS or the equivalent | Respondent: Representing the professional National Fertility Society members or Fertility specialist |
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| Korea | Seung-Yup Ku |
| Latvia | Dace Rezeberga |
| Libya | Abdul Khalig Ali Alzwe |
| Libya | Mohamad Mahaishi |
| Mexico | Alejano Badiola |
| New Zealand | John Peek |
| Norway | Arne Sunde |
| Panama | Roberto Epifanio |
| Peru | Soledad Sepúlveda |
| Philippines | Virgilio M. Novero Jr. |
| Portugal | Sofia Dantas |
| Russia | Vladislav Korsak |
| Russia | Anna Smirnova |
| Saudi Arabia | Samar Hassan |
| Senegal | Rokhaya Thiam Ba |
| Singapore | P C Wong |
| Slovenia | Tomaz Tomazevic |
| Spain | García Velasco Juancho |
| Spain | Charo Buxaderas Sanchez |
| South Africa | Silke Dyer |
| South Africa | Paul Le Roux |
| Sweden | KG Nygren |
| Switzerland | Gabriel de Candolle |
| Taiwan | Yung Kwei Soong |
| Togo | Kwasivi Moise Fiadjoe |
| Tunisia | Kharouf Mahmoud |
| Turkey | Ertan Kervancioglue |
| Uganda | Josaphat Byamugisha |
| United Kingdom | Alison Mctavish |
| United Kingdom | Allan Pacey |
| United Kingdom | Francoise Shenfield |
| United States | David Adamson |
| Uruguay | Rita Vernocchi |
| Venezuela | Francisco Risquez |
| Vietnam | Nguyen Viet Tien |

# Preface 2013

The current version of this IFFS Surveillance Report (Surveillance 2013) has undergone considerable evolution . The highly accomplished leaders, Drs. Howard Jones, Jr., Ian Cooke, Roger Kempers, and Doug Saunders, have retired from their editorial duties after committing over a decade to the inception, development, and production of the IFFS Surveillance Report. Their vision, insights, and extraordinary productivity made Surveillance an ongoing successful activity for IFFS. Of the 2010 editors, only Dr. Peter Brinsden has continued. A larger editorial board was assembled for this edition of Surveillance, and Paul Devroey and I were enthusiastically supported by the talented writing group of Drs. Manish Banker, Peter Brinsden, John Buster, Moïse Fiadjoe, Marcos Horton, Karl Nygren, Hirshikesh Pai, Paul Le Roux, and Elizabeth Sullivan. We wish to gratefully acknowledge the superb technical support and external review by Sheryl van der Poel from the World Health Organization. We also wish to thank the IFFS officers, Board of Directors, and administrative staff for their excellent support and assistance.

Surveillance remains a triennial report released on the occasion of the IFFS Congress. The transition of Surveillance to a Web-based survey progressed considerably for the 2013 edition. Redshift Technologies, a data management/IT firm, was engaged to develop and refine a custom online survey based on the previously used questionnaire with the intent to be accessible to all national society participants, worldwide. The advantages of this system included the ability to create a more user-friendly survey with internal validation systems and data analysis in place. The system created an enormous multinational database and facilitated the extraction of data for producing this report. It provided central data analysis immediately available to the editorial group. The Surveillance 2013 editors are very appreciative of Ethan Wantman at Redshift Technologies, whose imagination and energetic commitment to the project were essential to the report's completion. In addition, the editors are deeply indebted to Kathleen Miller who solved the hitherto insurmountable problem of converting the large cumbersome Excel spreadsheets into concise, legible, print format-ready tables. The current format and final product reflect the skill and thoroughness of our copy editor, Jill Vandermeulen.

For the Surveillance 2013 survey, requests to participate were emailed to 216 individuals who potentially represented over 150 countries. This list was primarily developed from past participants, who were contact sources representing the professionals from their respective National Societies. Ultimately, respondents from 60 countries who had partially or fully completed the survey provided sufficient information to be used in the analysis. The number of responses to individual questions from participants ranged from 0 to 205 with a minimum of 32 survey responses required for inclusion of their survey results in the report. Most of the chapters reflect a variable number of responses from the 73 respondents representing the 60 countries. Although the total number of respondents that logged onto the website was comparable to the response noted in the Surveillance 2010 survey, the 60 countries included this year are fewer than the 105 reported within the Surveillance 2010 but consistent with the 59 national participants in 2007. However, response rates for some topics, such as insurance coverage, were more extensive for this year's iteration. A

top priority for the next version will be to secure broader representation of additional National Fertility Societies or their equivalent through our status as a nongovernmental organization (NGO) in official relations with the World Health Organization (WHO).

Surveillance offers a snapshot of assisted reproductive technology (ART) *in vitro* fertilization (IVF) applications worldwide, as they existed in the fall of 2012. The data presented in this report, attests to consistencies in practice around the world and highlights local differences that reflect cultural, religious, and other preferences. The data compiled herein reflect the understanding of one or two well-informed individuals concerning the professional practice and status of ART within their country. As such, we acknowledge that there are likely intrinsic potential bias and errors of omission and commission that are inherent in this collection methodology.

Trends noted in the Surveillance 2013 depict a more modest growth in the number of new IVF facilities over previous intervals. Laws and guidelines enacted over the past three years seemed to have shown a significant (75% positive) salutary effect on the practice of ART. Although considerable variation in approaches to safety and quality control is noted by regulation or between professionals practicing in countries, there appears to be a consistent overall trend towards broader access to ART with increased safeguards for the stakeholders.

Steven J. Ory

Editor-in Chief, Surveillance 2013

# Chapter 1: Number of centers

## INTRODUCTION

Generating an accurate estimate of the number of IVF centers which provide ART in the world is problematic for a number of reasons. In countries in which clinics are registered, licensed, or otherwise regulated, reasonable calculations exist. However, some of the most populous countries do not have any relevant registries or have incomplete or inconsistent tallies/outcomes. Countries where a first IVF clinic is just being established may not be identified for this analysis, and the opening of new centers and closing of older ones is an ongoing dynamic process, worldwide.

## ANALYSIS OF THE SURVEY

The 2013 Surveillance survey was initiated in the fall of 2012, and invitations to participate were sent to 216 individuals. Ultimately, 73 responses representing expert-informed data from 60 countries, of which 59 provided information about the number of centers, were received and deemed sufficient for analysis (Table 1.1). In 2010, representatives from 104 countries provided data regarding the number of IVF units in their respective countries. One representative new to the survey provided data on Kazakhstan for the 2013 survey, and 45 previous participants did not. Despite the absence of data from the previous 45 participants, the survey notes that based only on participants from 60 countries, there is an increase in the total number of IVF centers, with most participants noting a modest increase in their total when compared to their 2010 tally. For the most part, the same respondents have provided the data in both survey years (2010 and 2013), and the changes noted may reflect genuine trends.

The current survey estimates that the number of IVF centers is approximately 3,706-3,895 compared to a range of 3,528-3,877 reported in 2010. The 45 participants in the 2010 study who did not contribute data this year accounted for approximately 550 centers that were cited in the 2010 total (thus unable to correct for new or clinic closures.) Nonetheless, these numbers are higher than the IVF Worldwide recent continent-by-continent estimate of 3,352 centers, which was an increase from the 3,055 total that they had noted in December 2009.

## REFERENCE

IVF Worldwide: http://www.ivf-worldwide.com/

| Table 1.1 Number of centers | | | |
|---|---|---|---|
| **Country** | **2010 (N)** | **2013 (N)** | **Comments** |
| Argentina | 23-25 | 30-44 | |
| Australia | 63 | Not reported | |
| Austria | 25 | 25 | |
| Belarus | 4 | 4 | |
| Belgium | 16-30 | 31 | |
| Brazil | 150 | 200 | |
| Bulgaria | 16 | 23 | |
| Cameroon | 2 | 2 | |
| Chile | 8-9 | 7 | |
| China | 102-300 | >200 | The number of centers approved by the Ministry of Health is about 200, but others are approved by health departments of provinces. |
| Colombia | 19-21 | 27 | |
| Croatia | 7-11 | 13 | |
| Czech Republic | 30 | 38 | |
| Democratic Republic of the Congo | 1 | 1 | |
| Denmark | 18-22 | 18-21 | |
| Dominican Republic | 4 | 5 | |
| Ecuador | 6-8 | 11 | |
| Egypt | 52-55 | 58 | |
| Finland | 19-20 | 18 | |
| France | 90-106 | 100 | |
| Greece | 50-60 | ~ 60 | |
| Hong Kong | 7 | 9-12 | |
| Hungary | 12 | 14 | |

| Table 1.1 Number of centers (continued) | | | |
|---|---|---|---|
| **Country** | **2010 (N)** | **2013 (N)** | **Comments** |
| Iceland | 1 | 1 | |
| India | 500 | 500-600 | |
| Ireland | 7 | 7-8 | |
| Israel | 24-30 | 29 | |
| Italy | 360 | 350 | |
| Ivory Coast | 3 | 2 | |
| Japan | 606-618 | 591 | |
| Kazakhstan | Not reported | 12 | |
| Latvia | 4-5 | 4 | |
| Libya | 9-10 | 8-10 | |
| Mexico | Uncertain | ~ 30 | |
| New Zealand | 7 | 7 | |
| Norway | 11 | 10 | |
| Panama | 7 | 9 | |
| Peru | 5-7 | 6 | |
| Philippines | 4 | 5 | |
| Portugal | 24 | 28 | |
| Russia | 80 | 110-130 | |
| Saudi Arabia | 24-30 | 30 | |
| Senegal | 2 | 2 | |
| Singapore | 9 | 11 | |
| Slovenia | 3 | 3 | |
| South Africa | 12-15 | 15 | |
| South Korea | 142 | 150 | |

| Table 1.1 Number of centers (continued) | | | |
|---|---|---|---|
| **Country** | **2010 (N)** | **2013 (N)** | **Comments** |
| Spain | 177-203 | >100 | |
| Sweden | 15-16 | 16 | |
| Switzerland | 26 | 26 | |
| Taiwan | 72-78 | 76 | |
| Togo | 1 | 1 | |
| Tunisia | 8 | 12 | |
| Turkey | 112-116 | 131 | |
| Uganda | 1 | 2 | |
| United Kingdom | 66 | 71 -117 | |
| Uruguay | 4 | 4 | |
| United States | 450-480 | 430 | |
| Venezuela | 17-18 | 10 | |
| Vietnam | 11-12 | 13 | |
| **Totals** | **3,524 - 3,870** | **3,701 - 3,890** | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 2: Legislation and guidelines

## INTRODUCTION

The practice of ART is extensively influenced by cultural, religious, and political exigencies in each of the locales in which it is practiced. All nations have a legitimate interest in promoting the safety and welfare of its citizens undergoing new medical therapy, and the practice of ART has endured special scrutiny in its regulation. The attention devoted to implementing new ART legislation appears to exceed that given to other medical disciplines. While the plethora of different national laws across the globe may try to ensure safety and implement best practices, they can be influenced by cultural norms, religious ideology, preferences of local officials, ethical opinion, and general public perception. For example, the Catholic Church's view, published in the 1987 "Donum Vitae" document, is that IVF is morally illicit; this view has profoundly influenced legislation in some countries. This position has not been modified. Other religions endorse IVF but are not supportive of certain applications such as use of donor gametes or surrogacy. ART practitioners and reproductive medicine societies have a unique insight into the field of IVF and infertility patients but often may have either a varied or limited role in the enactment of legislation promulgated in different countries.

The previous IFFS 2010 Surveillance Report documented an increase in ART legislation between 2007 and 2010. In countries where IVF has been more recently introduced, there is often no legislation or "quasi-legislation," but over time most countries appear to have either developed or have begun to develop guidelines and dedicated ART legislation. The intent of some forms of newer legislation has not, for example, been consistently realized and sometimes has produced unintended consequences, such as motivating patients to travel abroad in search of higher success rates or specific treatments otherwise unavailable, a practice that has been defined as "reproductive tourism" or "cross-border reproductive care."

Increased medical negligence claims, as well as harsher penalty violations for breach of ART law, has put pressure on ART clinicians and embryologists to be more vigilant and compliant with existing national guidelines and legal statutes. Guidelines at the Society level as well as national level, are often written to protect and guide ART practitioners with the intent to provide best practice and to better ensure avoidance of possible medical negligence claims.

This chapter surveys the global landscape with respect to legislation and guidelines and, in particular, addresses changes since the 2010 publication.

## ANALYSIS OF THE SURVEY

There were 73 respondents from 60 countries that contributed reliable data to this survey. Of these, 31% used only legislation to regulate ART, 21% used only guidelines to regulate ART, 37% used both legislation and guidelines, and 9% had neither regulations nor guidelines. See Table 2.1. There was a licensing body to regulate the practice of ART in 74% of the countries where participants were surveyed. There are various methods for the implementation of legislation, and the respondents were asked how clinical surveillance was carried out in their country. In 16%, an on-site inspection took place, 6% submit to a periodic report, 29% had both an on-site inspection and periodic reports, and 2% used other methods. In 24%, no surveillance was undertaken and it was unknown in 8%. In summary, approximately two thirds of the respondents replied that there were checks in place to implement enacted legislation directly with the practicing clinics.

There are penalties for violation of the statutes in 67% of the respondents' countries. In 54%, it was recorded that penalties are carried out by health officials, 17% by medical officials or unofficial agencies, and 20% by both health and medical officials. In 9%, the respondents did not know who enforced the penalties.

Laboratories are not always included in the surveillance of the ART clinics; therefore, respondents were asked separately about laboratory surveillance. However, the results obtained were similar to the clinical surveillance data. In this study, 77% had some form of surveillance (22% on-site inspection only, 8% periodic reports only, 31% both on site and periodic reports, and 16% other methods).

Laboratory accreditation was done in 69%, 65% had laboratory certification, and 68% had quality control systems. There were also specific penalty violations noted in the legislation for laboratory procedures in 57% of the respondents surveyed. Some countries used the International Organization for Standardization (ISO) accreditation system or complied with the European Union (EU) tissue directive legislation. Voluntary accreditation via a national reproductive society was reported as a common method of laboratory assessment.

In this 2013 survey, the respondents were asked about whether there had been an update in the legislation in 2012 since the previous IFFS surveillance data were collected in 2009. In 43%, there had been an update in the legislation. Where legislation was updated, 77% concluded that it has been an improvement, 5% a regression, and 18% had no opinion. In some countries, whole new Health Acts incorporating ART were introduced (e.g., South Africa and Russia). In other countries, specific legislation was introduced to address important issues; for example, in the United Kingdom, there was the introduction of legislation to increase donor compensation. In Brazil, Croatia, Taiwan, and Turkey, there were laws passed about the number of embryos to transfer. In August 2012, the European Court of Human Rights invalidated one provision of the restrictive Italian law on ART. The Court ruled that a part of the law prohibiting non-infertile couples from accessing embryo screening (preimplantation genetic diagnosis [PGD]) was a violation of the right to privacy and family life (1). In Argentina, Czech Republic, and Latvia, legislation relating to insurance or government payment toward IVF was instituted. Law on oocyte donation and sex selection was updated in Israel. In Denmark, anonymous and non-anonymous gamete donation was legalized, and single women were allowed access to treatment. In Belgium, the implementation of the EU tissue directive was implemented, which increased administrative costs but was of questionable benefit to patients.

Respondents were asked about the publicity given to penalty violations for breach in ART practice. Twenty-five percent of respondents replied that there was increased publicity given to the violations, 41% replied that there was no increase in publicity, and the remainder replied that it was not applicable or unknown. Penalties for failure to comply with ART legislation or guidelines varied from revocation of a physician's license to practice or deregistration of a clinic in some countries, to fines and imprisonment in other countries.

New legislation often devolves around well-known topics, and in this survey, China, India, South Africa, Argentina, Croatia, Belarus, and Czech Republic all had legislation introduced relating to the number of embryos that can be transferred. In Austria and Denmark, new legislation was introduced relating to single embryo transfer in IVF. In Belgium, there was no change in the restrictive 2003 law, but reimbursement is now linked to the number of embryos transferred. However, changes in legislation or guidelines regarding

other important key areas were infrequent. Only 22% of countries introduced new legislation relating to cryopreservation procedures, 8% for donor anonymity, and 4% for child welfare laws.

## DISCUSSION

ART remains a highly regulated medical discipline. In this survey, 90% of the respondents surveyed reported some regulation of ART via either legislation or guidelines or a combination of both. Legislation was updated in 43% of the respondent's countries, demonstrating the continued role of government in regulating the practice of ART. The ultimate benefit and harm of regulation continues to be intensely debated, but the widespread acceptance of the legitimacy of ART and society's role in promoting its safe and ethical application are now well established. Globally, there seems to be an emerging consensus regarding availability and best practices, although considerable regional variation still exists. The rapidly evolving technology and inherent ethical issues integrally associated with ART mean that some degree of guidance for physicians is essential. There will unfortunately always be some physicians who act unethically and merit sanctions, but the majority could be hindered by excessive restrictive oversight.

Some of the more controversial legislation enacted includes limits on the number of oocytes that can be fertilized and restrictions on use of donor oocytes and donor compensation. It was encouraging to note that 77% of countries replied that new legislation drafted in the last 3 years has improved existing legislation. There has been an increase in media attention for violations of ART legislation reported in 25% of the countries. This change in addition to the increase in public awareness of medical negligence litigation may be reassuring to the general public, but can also be destructive if it discourages transparency and responsible, corrective actions on the part of the clinics when errors and mishaps occur.

The high rate of 65%-75% for laboratory accreditation, certification, and surveillance also can be viewed as a positive development. This trend has continued and is now clearly international global norm.

## SUMMARY

The IFFS 2013 survey incorporated more detailed data being reported from respondents from 60 countries than in previous IFFS reports. Most countries used legislation, guidelines, or a combination to regulate ART practice (90%). In 43% of countries, there was a reported update in legislation over the last 3 years. There was evidence that the drafting and implementing of new legislation was often influenced by the views of religious ideology, politicians, and health officials rather than only medical personnel. There are trends identified that depict increased surveillance of IVF laboratories, stronger penalties for ART violations, and increased publicity of these violations. In two thirds of countries, IVF laboratories are accredited, are certified, and/or have surveillance by authorities.

## REFERENCE

1. http://www.presseurop.eu/en/content/news-brief/2601161-echr-condemns-italian-law-assisted-reproduction

| Table 2.1 Legislation and guidelines | | | | | |
|---|---|---|---|---|---|
| **Country** | **Legislation** | **Guidelines** | **Licensing body** | **Laboratory accreditation** | **New legislation since 2009** |
| Argentina | + | + | - | + | + |
| Australia | | | + | | |
| Austria | + | + | + | + | - |
| Belarus | + | + | + | - | - |
| Belgium | + | - | + | + | + |
| Brazil | + | + | + | + | + |
| Bulgaria | + | | + | + | + |
| Cameroon | - | + | - | + | + |
| China | + | + | + | + | - |
| Chile | - | - | - | + | - |
| Colombia | + | - | - | - | - |
| Croatia | + | - | + | + | + |
| Czech Republic | + | - | + | + | + |
| Democratic Republic of the Congo | - | - | - | - | - |
| Denmark | + | - | + | + | + |
| Dominican Republic | + | - | - | - | - |
| Ecuador | - | - | - | - | - |
| Egypt | - | + | + | + | - |
| Finland | + | - | + | + | - |
| France | + | + | + | + | + |
| Greece | + | - | + | + | - |

| Table 2.1 Legislation and guidelines (continued) | | | | | |
|---|---|---|---|---|---|
| **Country** | **Legislation** | **Guidelines** | **Licensing body** | **Laboratory accreditation** | **New legislation since 2009** |
| Hong Kong | + | + | + | + | - |
| Hungary | + | - | + | + | - |
| Iceland | + | - | + | - | - |
| India | - | + | - | + | - |
| Ireland | + | + | + | + | - |
| Israel | + | + | + | + | + |
| Italy | + | + | + | + | + |
| Ivory Coast | - | + | - | + | - |
| Japan | - | + | - | - | - |
| Kazakhstan | + | + | + | + | + |
| Korea | + | + | + | + | + |
| Latvia | + | + | + | - | + |
| Libya | + | - | + | - | - |
| Mexico | - | - | + | - | - |
| New Zealand | + | + | + | + | + |
| Norway | + | + | + | - | - |
| Panama | - | - | + | - | - |
| Peru | - | - | + | + | - |
| Philippines | - | + | - | - | - |
| Portugal | + | - | + | + | + |
| Russia | + | + | + | - | + |
| Saudi Arabia | - | - | - | + | - |

| | | | | | |
|---|---|---|---|---|---|
| Senegal | - | - | - | + | - |

**Table 2.1 Legislation and guidelines (continued)**

| Country | Legislation | Guidelines | Licensing body | Laboratory accreditation | New legislation since 2009 |
|---|---|---|---|---|---|
| Singapore | - | + | + | + | + |
| Slovenia | + | - | + | + | - |
| South Africa | + | + | + | + | + |
| Spain | + | + | - | - | - |
| Sweden | + | + | + | + | - |
| Switzerland | + | + | + | + | - |
| Taiwan | + | + | + | - | + |
| Togo | - | - | + | - | - |
| Tunisia | + | - | - | + | + |
| Turkey | + | + | + | - | + |
| Uganda | - | - | - | + | + |
| United Kingdom | + | + | + | + | + |
| Uruguay | - | - | - | - | - |
| United States | + | + | + | + | - |
| Venezuela | - | - | - | + | - |
| Vietnam | - | + | + | + | + |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 3: Insurance coverage

## INTRODUCTION

There is considerable international variability reported in the provision of insurance coverage for ART treatment among countries. This variability has persisted despite infertility being recognized as a major public health problem and being defined as a condition that leads to disability in the first WHO and World Bank Disability Report published in 2011. A recent study investigating the global trends and prevalence of infertility analyzed data from 277 demographic and reproductive health surveys and conservatively "estimated 48.5 million couples were unable to have a child after five years," demonstrating the burden of infertility worldwide in 2010 (1) with recognition that if the analysis evaluated a 2-year timeframe the estimate would be 2-2.5 times larger. This estimate in couples was based upon analysis of women, without an ability to directly estimate the male contribution. In 2010, almost one third (n=16/50) of participants representing 50 countries undertaking the IFFS Surveillance reported no insurance coverage for ART (2). This lack of coverage was not limited to low- and middle-income countries, with two high-income countries (Switzerland and Canada) reporting no national insurance coverage for ART treatment.

## ANALYSIS OF THE SURVEY

There are limitations in the completeness and quality of the 2013 survey data presented. There is variability in which countries are being represented by respondents to the 2013 survey compared to the 2010. Interpretation of the data should take into consideration the limitations of the data. Respondents from 60 countries provided information in the 2013 survey regarding medical insurance coverage for ART compared to respondents from 50 countries in 2010 (Table 3.1). Twenty-five new countries were represented by respondents providing data, most notably those reporting from India, Japan, Central and Latin America, and the Middle East (Table 3.2). In contrast, 14 of the 50 countries represented by respondents who had completed the survey in 2010 did not supply data in 2013, which includes Indonesia, Germany, the Netherlands, and Canada (Table 3.2). The variability in country respondents makes it difficult to draw conclusions from the data as to whether there have been global changes over the last 4 years in insurance coverage for ART. Of note, is that 9 of the 14 for which country data is not reported by respondents in 2013 but who had participated in the 2010 survey were from Europe. Among the 60 countries for which respondents had supplied information about insurance coverage, just over half (31/60) reported a national health plan (Table 3.2). The type of coverage of the national health plan was characterized as partial or complete. Of the 31 country respondents with a national health plan, almost three quarters (23/31) were characterized as partial and 26% (8/31) as complete (Table 3.2).

Countries with reported national health plans often had unique restrictions (Table 3.3). An age restriction was the most common requirement for accessing the national health plan, and for country respondents who provided this information, the age limit ranged from 38 to 44 years (Table 3.3). For Spain and Latvia, the limit reported was 40, or under 40 years respectively, and for South Korea, 44 years. The second most common restriction related to limitations of coverage for producing the first child, such as reported for Denmark, or limits on the total number of cycles offered, as reported for Portugal with 3 cycles, France, 4 cycles, and Hungary, 5 cycles. Notably, the number of cycles reported to be covered under the national health plan did not change between 2010 and 2013 in Portugal, France, and Hungary. Several of the countries' criteria that were reported to be required for funding included a combination of one or more factors such as parity, age, marital status, income, and number of cycles. For Slovenia, it was reported that there is funding of 6 cycles for the first baby and then 4 cycles after a live birth up to age 42 years. In contrast, it was reported that for Israel, funding ceased after 2 children were born. South Korea was

reported to provide partial coverage for married couples, aged ≤44 years with a family income less than 150% of the urban average, for 4 cycles of *in vitro* fertilization and 3 cycles of intrauterine insemination. A number of countries with national health plans were reported to have partial coverage, as in Sweden, where 60% of the total cost was funded through the government with 40% 'out of pocket' expenses paid by the couple, and in Norway, where patients were reported to be required to pay up to 2,500 euros for 3 treatment cycles. There were a number of countries within which respondents had reported a national health plan that had a limited number of cycles available nationally, such as Russia with 10,000 cycles in 2011 and 2012 and Kazakhstan with 700 cycles annually (Table 3.3). In 2010, Belgium was reported to be the only country with health insurance coverage dependent upon single embryo transfer for select populations. In 2013, the only country whose respondent reported a similar requirement was the Czech Republic with elective single embryo transfer (eSET) partially funded by the national health plan, whereby if eSET is used in the first 2 IVF cycles, there are 4 IVF cycles reimbursed with some additional 'out of pocket' expenses. Overall, respondents for 36 countries reported partial or complete coverage of ART treatment by a national health plan and/or private health insurance (Table 3.2). Only 9 (15%) respondents for countries reported coverage of ART treatment by private insurance; these included the United States, whose respondent reported variable private coverage nationally with some state-mandated coverage (Table 3.2). Respondents from Saudi Arabia and Libya reported full private health insurance coverage of ART treatment in the private sector (Table 3.3). In contrast, in the Philippines, only selected international health insurance providers were reported by respondents to include coverage of ART treatment (Table 3.3). Twenty-four (40%) countries were reported by respondents to have no health insurance coverage (Tables 3.1, 3.2). This included 3 of the most populous countries in the world, China, India, and Brazil, with other countries from Central and Latin America and Africa.

## DISCUSSION

The majority of respondents who had completed the survey had reported some form of public or private sector health insurance coverage for ART treatment. However, there was no consistent or standard eligibility criteria for accessing publicly funded ART treatment at a country level. Information on eligibility for private sector health insurance coverage ART treatment was not collected. There was a lack of information provided by respondents on whether policies around elective single transfer were associated with particular funding models for ART treatment. Interestingly, a number of populous countries, including Argentina, the United States, and Russia, were reported by respondents to have variable public sector insurance coverage at a regional, state, or provincial level. Compared to middle- and low-income countries, high-income countries with the main exception of the United States continued to be more likely to have national health plans with coverage for ART treatment. As detailed above, respondents from India, China, and Brazil have reported no public or private sector coverage of ART treatment, demonstrating the persisting inequity in access to ART treatment globally.

Caution should be taken when interpreting these data. There are marked limitations in the completeness and quality of the survey data presented, such as with the detailed comments about the eligibility criteria or requirements for funding. The variability in respondents from countries who provided feedback to surveys in 2010 versus in 2013 should be of concern for interpretation - particularly, the number of high-income countries not responding in the 2013 survey, which impacts the findings for these questions and ability to assess trends.

## SUMMARY

The availability of health insurance coverage for ART treatment varies markedly by country. Of the respondents providing feedback for 60 countries for the 2013 survey, 52% reported a national health plan

compared to 60% in 2010, perhaps reflecting the differences in respondents between surveys (loss of respondents from European countries) more than differences in the trends in national health plan coverage. The 2013 Surveillance shows that there remains enormous variability between countries regarding criteria for and extent of insurance coverage.

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3. http://www.iffs-reproduction.org/documents/IFFS_Surveillance_2010.pdf (International Federation of Fertility Societies Surveillance 2010. Jones HW, Cooke I, Kempers R, Brinsden P, Saunders D [eds]. Fertil Steril, 2010. doi:10.1016/j.fertnstert.2010.08.011).

| Table 3.1 Summary | | (N) | % |
|---|---|---|---|
| **Number of countries with respondents providing data in 2013** | | 60 | |
| **Number of countries with respondents providing data in 2010** | | 50 | |
| **Number of new countries with respondents in 2013** | | 25 | |
| **Number of countries that did not have respondents supplying data in 2013 who had in 2010** | | 14 | |
| **Proportion of countries from the 2010 Surveillance Report with some form of insurance** | | 64 | |
| | | | |
| **No coverage in 2013** | | 24 | 40 |
| **National plan in 2013** | Partial coverage | 23 | 38 |
| | Complete coverage | 8 | 35 |

## Table 3.2 Summary of responses: 2010 and 2013

| Country | Surveillance reporting year | | | Type of coverage | | | Type of coverage provided |
|---|---|---|---|---|---|---|---|
| | *First report 2013* | *No report 2013* | *Reported 2010 and 2013* | *National health plan* | *Private Insurance* | *No coverage* | |
| Abu Dhabi | | + | | | | | |
| Albania | | + | | | | | |
| Argentina | | | + | | + | | |
| Armenia | | + | | | | | |
| Australia | | | + | + | + | | Partial |
| Austria | | | + | + | | | Partial |
| Belarus | + | | + | | | + | |
| Belgium | | | + | + | + | | Partial |
| Brazil | | | + | | | + | |
| Bulgaria | | | + | + | | | Partial |
| Canada | | + | | | | | |
| Cameroon | + | | + | | | + | |
| Chile | + | | + | + | | | Complete |
| China | | | + | | | + | |
| Colombia | | | + | | | + | |
| Croatia | | | + | + | + | | Partial |
| Czech Republic | | | + | + | | | Partial |
| Democratic Republic of the Congo | + | | + | | | + | |
| Denmark | | | + | + | | | Complete |
| Dominican Republic | + | | + | | | + | |
| Ecuador | + | | + | | | + | |
| Egypt | + | | + | | | + | |
| Estonia | | + | | | | | |
| Finland | | | + | + | | | Partial |
| France | | | + | + | | | Complete |
| Germany | | + | | | | | |
| Greece | | | + | + | | | Partial |
| Hong Kong | | | + | + | | | Partial |
| Hungary | | | + | + | | | Complete |
| Iceland | | | + | + | | | Partial |
| India | + | | + | | | + | |
| Indonesia | | + | | | | | |
| Iran | | + | | | | | |
| Ireland (Republic) | + | | + | | | + | |
| Israel | | | + | + | | | Complete |
| Italy | | | + | + | | | Partial |
| Ivory Cost | + | | + | | | + | |
| Japan | + | | + | + | | | Partial |
| Kazakhstan | + | | + | + | | | Partial |
| Kosovo | | + | | | | | |
| Kuwait | | + | | | | | |
| Latvia | | | + | + | | | Partial or complete if age limit |
| Libya | + | | + | | + | | Complete |
| Mexico | + | | + | | | + | |
| Montenegro | | + | | | | | |
| New Zealand | | | + | + | | | Partial |
| Netherlands | | + | | | | | |
| Norway | + | | + | + | | | Partial |
| Panama | + | | + | | | + | |
| Peru | + | | + | | | + | |
| Philippines | + | | + | | + | | Partial |
| Portugal | | | + | + | | | Partial |
| Romania | | + | | | | | |
| Russian Federation | | | + | + | | | Complete |
| Saudi Arabia | + | | + | | + | | Complete |
| Senegal | + | | + | | | + | |
| Singapore | + | | + | + | | | Partial |
| Slovakia | | + | | | | | |
| Slovenia | | | + | + | | | Complete |
| South Africa | | | + | | | + | |
| South Korea | | | + | + | | | Partial |
| Spain | | | + | + | + | | Complete |
| Sweden | | | + | + | | | Partial |
| Switzerland | | | + | | | + | |

## Table 3.2 Summary of responses: 2010 and 2013 (continued)

| Country | Surveillance reporting year | | | Type of coverage | | | Type of coverage provided |
|---|---|---|---|---|---|---|---|
| | *First report 2013* | *No report 2013* | *Reported 2010 and 2013* | *National health plan* | *Private Insurance* | *No coverage* | |
| Taiwan | | | + | | | + | |
| Togo | + | | + | | | + | |
| Tunisia | | | + | + | | | Partial |
| Turkey | | | + | + | | | Partial |
| Uganda | + | | + | | | + | |
| United Kingdom | | | + | + | | | Partial |
| Uruguay | + | | + | | | + | |
| United States | | | + | | + | | Partial |
| Venezuela | + | | + | | | + | |
| Vietnam | | | + | | | + | |
| Total | 25 | 14 | 60 | 31 | 9 | 24 | |

* Multiple replies submitted for the country but only one response included in table.

| Table 3.3 Comments from respondents in individual countries (restrictions) | | | |
|---|---|---|---|
| **Country** | **Change from 2010** | **2010 comments** | **2013 comments** |
| **Abu Dhabi** | National plan | | |
| **Albania** | No coverage | | |
| **Argentina** | | | Some provinces have their own statutes, with partial or total coverage depending on female age, type of insurance, and number of cycles. |
| **Armenia** | No coverage | | |
| **Australia** | National plan | Under the Australian Medicare system, each patient receives a set amount of reimbursement towards the cost of an ART cycle | |
| **Austria** | National plan | | Two thirds of cost covered by national health system |
| **Belgium** | National plan | | Regulated by law |
| **Brazil** | No coverage | | High costs |
| **Bulgaria** | National plan | | IVF/ICSI fully reimbursed up to 3 cycles and 2,500 euros. All additional procedures (AH, MACS, cryostorage, and use of anonymous donor sperm) and IUI are not reimbursed. |
| **Canada** | No coverage | | |
| **Chile** | | | Covers 15% cost of a cycle, the difference is out-of-pocket funding |
| **China** | No coverage | | No coverage |
| **Colombia** | No coverage | | |
| **Croatia** | National plan | | |
| **Czech Republic** | National plan | | Elective single embryo transfer is supported by health care insurances. If eSET in the first 2 IVF cycle, 4 IVF cycle reimbursed (not completely). Some procedures (ICSI, PICSI®, embryo freezing, frozen embryo transfer, extended culture) and medication copayment always have to be paid by an infertile couple (48/1997 coll. Upgraded by 369/2011 coll.) |
| **Denmark** | National plan | | The reimbursement is only possible for the first child and the woman has to be below 40 years of age. For the second child, the couple has to pay full price for the treatment in a private clinic, but there is still a reimbursement part for the medication. |
| **Estonia** | National plan | 100% treatment/60% medication | |
| **Finland** | National plan | | Medication partly covered (both private and public clinics), public clinics cover 40% of ART cycles, private treatments partly reimbursed by the social insurance (up to age of 42 years) |
| **France** | National plan | | Limitation to 4 cycles |
| **Germany** | National plan | 50% costs of 3 cycles | |
| **Greece** | National plan | Complete coverage by the law | Medication expenses (under conditions and with patient contribution) and approximately 350 euros towards medical and laboratory expenses |
| **Hong Kong** | National plan | | Up to 3 IVF cycles can be funded to women up to the age of 40. Note second answer: 3 public hospitals provide subsidized ART treatment for patients with primary infertility younger than 38 years. |

| Table 3.3 Comments from respondents in individual countries (restrictions) (continued) | | | |
|---|---|---|---|
| **Country** | **Change from 2010** | **2010 comments** | **2013 comments** |
| **Hungary** | National plan | | 5 cycles with ET are totally covered independent from the number of earlier pregnancies. Drugs are reimbursed from 0% to 70%. GnRH analogues: 0%, FSH/hMG, LH: 70%, progesterone: 30% |
| **Iceland** | National plan | | |
| **Indonesia** | No coverage | | |
| **Iran** | No coverage | | |
| **Ireland (Republic)** | | | Only the cost of drugs is covered (with the exception of 130 euro to be paid by patient). ART treatments are not financially supported by state or health insurance. |
| **Israel** | National plan | Coverage until 2 live births | If, according to IVF law, special medical indications |
| **Italy** | National plan | | Treatments performed within the national health care system are totally or partially reimbursed (according to criteria defined by each region). The budget available at a national level, however, can only cover 50% of treatments. |
| **Japan** | | | Partial reimbursement is available from the local governments. |
| **Kazakhstan** | | | 700 cycle per year |
| **Kosovo** | No coverage | | |
| **Kuwait** | No coverage | | |
| **Latvia** | No coverage | | 50 cycles in 2012. Woman age until 38. Program started only in November 2012 - women age limit until 38 years |
| **Libya** | No coverage | | All centers are private |
| **Montenegro** | National plan | | |
| **New Zealand** | | | Full cover if people meet eligibility criteria. |
| **Netherlands** | National plan | Mandatory private health insurance | |
| **Norway** | | | At governmental units: patients pay up to 2,500 euro (Norwegian krone 19,000) for up to 3 treatment cycles |
| **Philippines** | | | Only a few international health insurances cover ART |
| **Portugal** | National plan | Totally supported in public sector - fee for service in the private | Maximum of 3 treatments |
| **Romania** | National plan | 2010 250 couples up to 2,000 euro entry criteria | |
| **Russian Federation** | National plan | For 5% of cycles in country, variable coverage | The federal government paid for 10,000 cycles in 2011 and 2012. It was done 31.6% cycles of ART in state clinic (from total 39,988 cycles in the country). Most of them were paid from regional or federal budget. |
| **Singapore** | | | Up to 3,000 Singapore dollars per stimulated cycle to Singapore citizens under the age of 40 undergoing IVF in a public hospital. |
| **Slovakia** | National plan | | |
| **Slovenia** | National plan | 6 cycles until age 42 years | 6 cycles for the first baby then 4 cycles after a live birth up to age of 42 years |
| **South Africa** | No coverage | ART subsidized in academic institutions, very limited private coverage | Patients all pay cash for procedures |
| **South Korea** | | Partial coverage criteria | Reimbursement by government: Partial coverage for 4 cycles of IVF and 3 cycles for IUI. Only under preconditions: Couple in marriage, age 44 years old or younger, and family income less than 150% of urban average |
| **Spain** | National plan | | Government covers IVF cycle until age 40. Some private insurances also cover the complete IVF cycle. |
| **Sweden** | National plan | Complete coverage for public hospitals, partial at clinics | 60% of the total cost in Sweden is paid publicly, 40% private money "out of pocket." No private insurance |

| Table 3.3 Comments from respondents in individual countries (restrictions) (continued) | | | |
|---|---|---|---|
| **Country** | **Change from 2010** | **2010 comments** | **2013 comments** |
| **Switzerland** | No coverage | | |
| **Taiwan** | No coverage | | |
| **Tunisia** | No coverage | Medicine expenses are covered for patients having public care | |
| **Turkey** | National plan | | |
| **Uganda** | | | Private |
| **United Kingdom** | National plan | Variable coverage | There are national guidelines produced by the National Institute for Health and Clinical Excellence (see http://www.nice.org.uk). These are currently being updated, but at the time of submissions were not yet available. Funding through National Health Service is variable throughout the UK. Postcode lottery still in place. |
| **United States** | Private insurance | Variable coverage with some coverage for diagnostic tests but not for treatment | Very uneven with excellent coverage in a few states, moderate in several, and poor in the majority. Some state-mandated coverage and then private coverage that is highly variable. |
| **Vietnam** | No coverage | Cost of ART very high | In our country, there is no coverage by any insurances. |

* Multiple replies submitted for the country but only one response included in table.

IVF = *in vitro* fertilization; ICSI = intracytoplasmic sperm injection; AH = assisted hatching; MACS = magnetic-activated cell sorting; IUI = intrauterine insemination; eSET = elective single embryo transfer; ET = embryo transfer; GnRH = gonadotropin-releasing hormone; FSH = follicle-stimulating hormone; hMG = human menopausal gonadotropin; LH = luteinizing hormone; ART = assisted reproductive technology

# Chapter 4: Marital status

## INTRODUCTION

This chapter deals with the issue of marital status of the couple as it relates to availability of ART services.

- The purpose of this survey question was to determine if there is a law or a guideline governing the practice of ART as it relates to the marital status of a couple.
- We also wanted to know what types of relationships between two individuals are allowed for the intervention of ART.

Some countries were reported to limit ART services to couples in a "stable relationship." Although this concept was widely embraced, there is no clear definition of relevant criteria for application. Although most countries were reported to now have laws or guidelines in place for the governance of ART, there are still 9 countries for which respondents claim that they do not have either.

We have divided the countries for which respondents replied into 5 categories: those in which marriage is a requirement, those that treat couples who are unmarried but in a stable relationship, countries permitting treatment of single persons, countries allowing lesbians to utilize ART services, and countries that had no requirements. These countries were also divided into subgroups based on how ART was reported to be governed in each place: by statutes, guidelines, both, or neither.

## ANALYSIS OF THE SURVEY

Respondents from 62 countries filled out the survey either partially or completely (Table 4.1). Forty-five countries were reported to mention that marriage was required for ART treatment, of which 13 countries have been reported to have requirements that state this as an absolute prerequisite; these countries are mainly Islamic and Southeast Asian. Thirty-three countries were reported to allow a stable relationship to be the criterion for receiving ART treatment. Twenty-six countries were reported to allow singles and 14 countries, those individuals identifying themselves as lesbian to receive ART treatment.

In some countries, like the United States, marital status was reported to not be considered before offering treatment. In the table, we also have included countries where there was a reported discrepancy in the response from two different respondents within the same country. These have been marked in the table for reference.

## SUMMARY

Strict requirement of marriage is reported to be present in a small number of countries, mainly Islamic and Southeast Asian. Nearly 40% of countries with respondents providing input allowed singles to undergo ART and more than 20% allowed lesbians to undergo ART. This trend in access to ART appears to be increasing.

| Table 4.1 Marital status | | | | | |
|---|---|---|---|---|---|
| **How ART is governed** | | | | | |
| ***Statutes/law*** | **Marriage required** | **Stable relationship** | **Singles permitted** | **Lesbians permitted** | **No requirements** |
| Belgium | + | + | + | + | |
| Bulgaria | + | + | + | + | |
| Croatia | + | + | | | |
| Czech Republic | + | + | | | |
| Denmark | + | + | + | + | |
| Finland | + | + | + | + | + |
| Greece | | + | + | | |
| Hungary | + | + | + | | |
| Ireland | | | | | + |
| Latvia* | + | + | + | + | |
| Libya* | + | | | | |
| Russia | + | + | + | | |
| Slovenia | | + | | | |
| Tunisia | + | | | | |
| United Kingdom | | + | + | + | |
| ***By guidelines*** | **Marriage required** | **Stable relationship** | **Singles permitted** | **Lesbians permitted** | **No requirements** |
| Cameroon | | | | | |
| Egypt | + | | | | |
| Hong Kong* | + | | | | |
| India | + | + | + | | |
| Ireland | | + | | | |
| Ivory Coast | + | + | + | | |
| Japan | + | | | | |
| Philippines | + | | | | |
| Singapore | + | | | | |
| Venezuela | + | | | | |
| Vietnam | + | | + | | |
| ***By both*** | **Marriage required** | **Stable relationship** | **Singles permitted** | **Lesbians permitted** | **No requirements** |
| Argentina | + | + | + | + | + |
| Austria | + | + | | | |
| Belarus | + | + | + | | |
| Brazil | + | + | + | + | |
| China | + | | | | |
| France | | + | | | |
| Israel | + | + | + | | |

| Table 4.1 Marital status (continued) | | | | | |
|---|---|---|---|---|---|
| **How ART is governed** | | | | | |
| Italy | + | + | | | |
| Kazakhstan | + | | + | | |
| ***Statutes/law*** | **Marriage required** | **Stable relationship** | **Singles permitted** | **Lesbians permitted** | **No requirements** |
| New Zealand | + | + | + | + | + |
| Norway | + | + | | + | |
| Russia | + | | + | | |
| South Africa | | | + | + | + |
| South Korea | + | | | | |
| Spain | + | + | + | + | |
| Sweden | + | + | | + | |
| Switzerland | | + | | | |
| Taiwan | + | | | | |
| Turkey | + | | | | |
| United States | | | | | + |
| ***By neither*** | **Marriage required** | **Stable relationship** | **Singles permitted** | **Lesbians permitted** | **No requirements** |
| Democratic Republic of the Congo | + | + | + | | + |
| Dominican Republic | | | | | + |
| Mexico | | | | | + |
| Peru | + | + | + | | |
| Saudi Arabia | + | | | | |
| Senegal | + | | | | |
| Togo | + | + | | | |
| Uruguay | + | + | + | + | |
| Venezuela | + | + | + | | |
| ***Unknown/null*** | **Marriage required** | **Stable relationship** | **Singles permitted** | **Lesbians permitted** | **No requirements** |
| Australia | | + | + | + | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 5: Number of embryos for transfer in IVF/ART

## INTRODUCTION

The world's first baby conceived by IVF in 1977 was the result of an oocyte retrieval following an unstimulated 'natural cycle' and the transfer of a single embryo. As the practice of IVF became advanced, it was recognized that ovarian stimulation with gonadotropins produced more oocytes and embryos and, with transfer of two or more embryos, an enhanced chance of achieving pregnancy. However, the cost of this strategy soon became apparent in that larger numbers of twins, triplets, and higher order multiple births resulted. Concern has since grown about the consequences of this policy, both to the babies born and to their parents.

The incidence of twin and high-order multiple births has quadrupled since 1980. This very significant increase has been attributed to three major factors: the delay of first childbirth with a corresponding higher incidence of multiple pregnancy in women of advanced maternal age, the increased use of ovulation induction and insemination procedures for infertile patients, and the more prevalent use of IVF.

The risk of fetal, neonatal, and infant death is considerably increased for twins, triplets, and quadruplets. The perinatal mortality and infant mortality rates for triplets were 164.5 and 147.7 per thousand live births respectively for England and Wales compared with mortality rates of 13.8 and 11.7 per thousand singleton births in 2007. For quadruplets, the mortality rate was 40%-50% higher than for triplets. This increase in perinatal mortality is primarily due to premature delivery, but also to utero-placental compromise and an increased rate of congenital anomalies among these infants. Maternal complications of triplet and high-order multiple births include pregnancy-induced hypertension, antepartum and postpartum hemorrhage, and severe anemia.

During the past 10 years, these risks have become more widely acknowledged and many countries have established either legislation or guidelines with the intent of limiting the number of embryos for transfer. Studies from Sweden, Denmark, the Netherlands, and Belgium have shown that single embryo transfer, especially when combined with frozen/thawed embryo transfer in subsequent cycles, achieves pregnancy and live birth rates equivalent to the transfer of two and even three embryos, without the complications of twin and higher order pregnancies and births. Several countries now have firm guidelines or regulations permitting only single embryo transfers for certain categories of patients. In the United Kingdom, the regulatory body has put in place measures to ensure that national and clinic-specific multiple pregnancy rates will be maintained below 10% of all IVF births.

Below and in Table 5.1 are the data from the IFFS survey, which show the strategies that have been reported that various countries have undertaken to control the high incidence of multiple pregnancies from IVF/ART.

### Indications for Single Embryo Transfer (SET)

The American Society for Reproductive Medicine (ASRM) in their recent Practice Committee Report on SET (2012) recommended the following as indications for SET:

- Female age <35
- More than one 'top-quality embryo' available for transfer
- First or second treatment cycle

- Previous successful IVF cycle
- Recipient of embryos created from donor oocytes

Some European countries are recommending even tighter criteria for SET, setting the age for SET at <37 or 38. The British Fertility Society (BFS) in 2008 recommended that at least 50% of embryo transfers should be SET, which would bring the multiple pregnancy rate down to <10%, and that practitioners should be guided by the following:

- Female partner's age
- Previous pregnancies
- Cause of infertility
- Number of previous IVF failures
- Response to follicular stimulation
- Number of oocytes
- Number of good-quality embryos
- Number cultured to blastocyst

## ANALYSIS OF THE SURVEY

The questions asked in this 2013 IFFS survey were:

- Are there guidelines or laws governing the number of embryos that can be transferred (in your country)?

- Do any guidelines specify the number of pre-embryos that can be transferred (replaced)?

Fifty-eight countries had respondents who provided responses to these questions. Of the 58 replies to the first question, 22 (38%) stated that they have guidelines or laws governing SET, 36 (62%) stated they do not have guidelines or laws, and 2 gave non-valid replies. Of the 60 countries that had respondents who provided replies to the second question, 37 (64%) said that they do have guidelines on the number of embryos to transfer. Further breakdown of the replies to both questions shows the following respectively: yes/yes 15 (26%), yes/no 11 (19%), no/yes 18 (31%), no/no 16 (28%), and invalid or not known 8 (14%). The surprising figure among these is the no/yes reply of 31%, which shows that these countries are reported to have no regulation or guidelines, but that guidelines do specify the number of embryos to transfer; one must assume that these responses are due to a misunderstanding of the questions.

Table 5.1 shows the country-by-country breakdown of policies being reported on the number of embryos for transfer, with comments by some respondents. The accuracy of the replies cannot be confirmed as we have relied on individuals' responses and have listed only one response per country.

## SUMMARY

In the 2010 IFFS survey, the question about the number of embryos that can be transferred was not asked, and so it is not possible to make any comparison with this latest survey. It is obvious, however, from reviewing the literature over the past 5 and more years, that there is an increasing awareness of the problems associated with multiple embryo transfers. More and more clinics worldwide are restricting the number of transferred embryos to one or a maximum of two.

In the future, it is probable that the success of IVF will improve, with improved culture systems and stimulation protocols. As this evolves, the current trend of limiting the number of embryos for transfer to one or two at the most will likely accelerate. Increasingly, the best measure of a clinic's success rate will be the implantation rate (chance of a single embryo implanting and developing) rather than pregnancy rate, which is more easily influenced by the number of embryos transferred. The recommendation that is being reported in many countries is now and increasingly will be in the future: "Transfer as many embryos as you like, but one at a time."

| Table 5.1 Guidelines and laws addressing number of embryos transferred | | | | |
|---|---|---|---|---|
| **Country** | **Yes** | **No** | **Null/ Unknown** | **Comments** |
| Argentina | + | | | At least 60% of embryo transfers must be of 2 or less embryos |
| Australia | + | | | One fresh embryo in first treatment cycle for less than 35 years old. Maximum of 2 embryos if over 38. |
| Austria | + | | | Reinforcement of SET in young patients. No more than 2 embryos for ET up to age 35 and first attempt up to 40 (ET of 3 only after repeated failures. From 40 years on 3 and more allowed for ET. |
| Belarus | + | | | 2 for younger than 35, older or in case of 3 failed IVF before - only 3 |
| Belgium | | + | | |
| Brazil | + | | | 2 embryos<35, 36-40 2 or 3, >40 3 or 4 |
| Bulgaria | + | | | From 1 to 3 embryos, very occasionally up to 4. There are specific rules depending on the embryo stage, AH, maternal age, number of attempts, etc. |
| Cameroon | + | | | No more than 3 embryos |
| Chile | | + | | |
| China | + | | | The number of embryos transferred should not exceed 3 each cycle. Women under 35 should not exceed 2. |
| Colombia | | + | | |
| Croatia | | | Unknown | |
| Czech Republic | + | | | Two frozen/thawed embryos are recommended to be transferred, but in older women, more can be transferred. |
| Democratic Republic of the Congo | | + | | |
| Denmark | + | | | Women below 40 years of age maximum of 2 embryos. Women above 40 years of age maximum of 3 embryos. |
| Dominican Republic | | | Unknown | |
| Ecuador | | + | | |
| Egypt | + | | | Women below 35 with no previous failures: 2 embryos. Age > 35 or with previous failure: 3 embryos. Age > 40: 4-5 embryos. |
| Finland | | + | | |
| France | + | | | Maximum 3. Need to document the choice. |
| Hong Kong | + | | | Usually up to 3; 4-5 in women >35 or with repeated implantation failure |
| Hungary | + | | | </= age 40 years 3 embryos, over 40 years 4 embryos, after 3 unsuccessful IVF 4 embryos |
| Iceland | + | | | |
| India | + | | | 3 embryos. More than 3 embryos in older patients or patients with repeated failures. |
| Ireland | | + | | |
| Israel | + | | | 1, medical exception |
| Italy | | + | | |
| Ivory Coast | | + | | |
| Japan | + | | | SET is mandatory for the patients under 35 of female age for the first and second ET attempt. The maximum number of embryos transferred is 2. |
| Kazakhstan | | + | | |
| Latvia | + | | | Not more than 3 embryos. Guidelines are under preparation and accept procedure. |
| Libya | | + | | |
| Mexico | | + | | |
| New Zealand | + | | | As for Part 2 |
| Norway | | + | | |

| Table 5.1 Guidelines and laws addressing number of embryos transferred (continued) | | | | |
|---|---|---|---|---|
| **Country** | **Yes** | **No** | **Null/ Unknown** | **Comments** |
| Panama | | | Unknown | |
| Peru | + | | | REDLARA (Latinoamericana de Reproducción Asistida) suggests no more than 3 embryos. |
| Philippines | + | | | 3 embryos, except for advanced age (over 38) where up to 5 embryos may be allowed (cleavage stage) |
| Portugal | | | Null | NULL |
| Russian Federation | + | | | 1 or 2 embryos. Informed consent form should be signed by patient in case of transfer of 3 embryos. |
| Saudi Arabia | | | Unknown | NULL |
| Senegal | | + | | NULL |
| Singapore | + | | | 2 embryos |
| Slovenia | + | | | Maximum 3 embryos by law. Maximum 2 by practice. Single in favorable cases less than 35 years of age, first 2 attempts. |
| South Korea | + | | | By the guideline of national health care plan (culture for 2-4 days) under 35 years of age: 2-3; 35-39; 3-4 over 39; (culture for 5-6 days) under 35: 1-2; 35-39; 2-3 over 39; 3 |
| Spain | + | | | Maximum 3 by law but depending on woman's age and number of high-quality embryos |
| Sweden | + | | | Law and guidelines state the same: 1 as a rule, exceptionally 2, never 3 or more |
| Switzerland | + | | | Maximum 3 |
| Taiwan | + | | | |
| Togo | | + | | |
| Tunisia | | + | | |
| Turkey | + | | | 1 embryo should be transferred; only exceptions for 2 embryos are either woman's age over 35 or previous 2 unsuccessful ART trials. |
| Uganda | | | Unknown | |
| United Kingdom | + | | | 2 embryos maximum before age 40 |
| Uruguay | | + | | |
| United States | | + | | |
| Venezuela | | + | | |
| Vietnam | | + | | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 6: Cryopreservation

## INTRODUCTION

The major aim of cryopreservation is to make the gametes available for future use by individuals or couples undergoing infertility treatment or fertility preservation procedures. Additionally, in patients with moderate/severe ovarian hyperstimulation syndrome (OHSS) or in those with poor endometrial receptivity, one can freeze the embryos and transfer them in subsequent frozen thaw cycles. In patients undergoing preimplantation genetic diagnosis/screening, using trophectoderm biopsy and array comparative genomic hybridization (CGH), blastocysts can be frozen to allow time to await results of the genetic test prior to transfer (1).

There is evidence of moderate quality that the implantation, clinical, and ongoing pregnancy rates of ART cycles may be improved by performing frozen embryo transfer compared with fresh embryo transfer, by improved embryo-endometrium synchrony achieved with endometrium preparation cycles (2). Although blastocyst transfer offers several theoretical advantages over the transfer of cleavage-stage embryos, the cumulative clinical pregnancy rates from cleavage-stage embryos (derived from fresh and thaw cycles) resulted in higher clinical pregnancy rates than from blastocyst cycles (3). On the other hand, in cases of elective single embryo transfer, it is preferable to transfer blastocysts.

In general, fewer embryos are available to freeze with blastocyst transfer compared with cleavage-stage transfer, and vitrification may result in more consistent survival rates and higher cumulative pregnancy rates compared to slow freezing (4). Fresh blastocyst transfer produces a better live birth rate than that achieved by transfer of blastocysts cultured from thawed cleavage-stage embryos. Freezing at the early cleavage stage and then thawing leads to better live birth rates than freezing at the blastocyst stage and then thawing for replacement (5). If vitrification was the technique used for freezing these cleavage-stage embryos rather than slow freezing, then the post-thaw blastocyst development is better. Embryos that were twice-frozen-thawed retained high viability and resulted in normal live births after thaw-ET, at a frequency comparable with that of once-frozen-thawed embryos (6).

Slow freezing that was formerly the norm is now being supplanted by vitrification, which has a well-documented higher success rate, can be accomplished with simpler equipment, and is technically easier and quicker to perform. Survival rate, fertilization rate, and implantation rate with vitrification are superior to the slow freezing method (7). Slow freezing or vitrification of oocytes have both shown comparable fertilization, pregnancy, and implantation rates in some reviews, but vitrification is preferred because of its simplicity (8).

Preliminary data regarding the safety of oocyte cryopreservation are reassuring, and the procedure is no longer considered to be experimental. There is good evidence that fertilization and pregnancy rates are similar with fresh oocytes or frozen thawed oocytes. No increases in chromosomal abnormalities, birth defects, or developmental deficits have been noted in the children born from cryopreserved oocytes. Oocyte freezing has developed substantially, finding wider applications and use. There are not yet sufficient data to recommend oocyte cryopreservation for the sole purpose of circumventing reproductive aging in healthy women (9).

Oocyte freezing has simplified the oocyte donation procedure. Furthermore, it may be a means of conserving potential fertility in women with malignancy. Preservation of immature oocytes should preferably be after maturation *in vitro* (10).

Among the established methods of trying to preserve fertility in women with cancer, in the postpubertal age group oocyte cryopreservation is the preferred option, whereas, for prepubertal girls ovarian tissue cryopreservation is generally the only option being considered. Ovarian tissue cryopreservation before treatment for malignancy is being practiced and has led to a small number of live births following transplantation. The procedure of ovarian tissue cryopreservation has been found to be safe, relatively simple, and promising (11).

Sperm cryopreservation is an established procedure and has remained a standard technique for donor insemination and for male fertility preservation in adult males with malignancy. Attempts are also being made to cryopreserve the small number of sperm from subfertile and infertile men, which may reduce the need to have recourse to surgical procedures or donor sperm. Sperm also can be frozen using the freeze-drying technique of lyophilization. This can preserve sperm for long periods of time at a fraction of the cost of current methods, without affecting sperm DNA integrity (12).

Sperm obtained from microsurgical epididymal sperm aspiration (MESA) or percutaneous epididymal sperm aspiration (PESA) can be effectively frozen. Thawing these sperm and using them for ICSI have shown results comparable to those using freshly retrieved sperm. Testicular tissue can be cryopreserved following testicular sperm aspiration (TESA), testicular sperm extraction (TESE), testicular surgery for undescended testes, or malignancy. The tissue can be thawed in the future and the isolated sperm can be used later for intracytoplasmic sperm injection (ICSI). Methods to protect future spermatogenesis by preserving immature testicular tissue in prepubertal boys suffering from malignancies are yet experimental.

## ANALYSIS OF THE SURVEY

ART legislation and guidelines regarding cryopreservation are being constantly updated and modified in countries all over the world (Tables 6.1-6.5). There have been such modifications reported in 22 of the 60 participating countries and respondents from 17 of these countries found these to be an improvement. Embryo cryopreservation legislation or guidelines have been modified in 11 countries. Fourteen countries are reported to be governed by statute law, and activities are conducted within guidelines in a further 10 countries and under both statutes and guidelines in 23 countries. There are neither laws nor guidelines in 12 countries, and in one country, Uganda, the respondent reported that it is unknown what governs the ART practice.

Cryopreservation of fertilized eggs (from prezygotes to blastocysts) is reported to be allowed by law in 39 countries and by guidelines in 44 countries. Ovarian or testicular tissue cryopreservation is reported to be permitted by the law in 32 countries and by guidelines in 35 countries. Oocyte preservation is permitted in 42 countries.

The duration of storage of fertilized eggs varies, and many (45%-50%) countries have been reported to have reached a consensus regarding the limit to this duration: The duration of storage is limited to 5 years in Argentina, Bulgaria, Denmark, Egypt, France, Hungary, Israel, Norway, Singapore, Sweden, Switzerland, and Turkey; an additional 5 years may be possible on request in India, Belgium, Korea (extension for cancer patients), Slovenia, and Tunisia. The limit is 2 years in Hong Kong for embryos

created by designated donation of gametes, but is 10 years in Austria, Australia, Hong Kong (own gametes and anonymous donor gametes), Hungary, Latvia, Taiwan, the United Kingdom, and New Zealand. In New Zealand, it was reported that the time may be extended further on application to an ethics committee. In the United Kingdom, storage can be extended beyond 10 years in exceptional circumstances, but the transfer should occur before the female partner reaches age 50. In the Czech Republic, it was reported that storage duration is 12 years. In Japan, clinics can store embryos during the period of marriage of the couple and during the reproductive age of the female patients, and in Spain, storage may last until the end of the reproductive years. Guidelines in the United States and in South Africa are reported to state that storage can be for an unlimited time, but unclaimed embryos should be discarded after 10 years. In Finland, Kazakhstan, and Peru, there was no reported limit.

Venezuela is the only country to report the prohibition of cryopreservation of embryos, but freezing of oocytes and ovarian or testicular tissue are permitted. In Ivory Coast and Vietnam, though reported to be permitted, embryo freezing is not practiced. In Croatia, it was reported that it is no longer forbidden, and surplus embryos may be frozen. In Italy, embryo cryopreservation is permitted only in specific cases. Although Ireland has no consensus as to the duration of storage, two non-specific changes occurred in 2009 that have indirectly altered practice: first, the Supreme Court judgment that embryos in storage are not guaranteed a right to life in the Irish Constitution (Nov 2009), and second, the Medical Council Guidelines no longer prohibit destruction of fertilized ovum.

Consent from both the partners has been reported to be required in most countries. In Hong Kong, application is restricted to married couples. In Belgium, the frozen embryos have to be used before creating new embryos. In Argentina, it is reported that centers must show consents with information regarding final destination of cryopreserved material. It was reported for Colombia, that the couple must undergo the infectious disease tests prior to the storage of their embryos. In the Czech Republic, storage was reported to be permitted in the closed system only.

There are 42 countries that were reported to permit oocyte cryopreservation and none that expressly prohibit it, although Uganda had not reported any such developed programs, as of yet. The indications permitted are reported to be specific in Venezuela. Fertility preservation is reported to be permitted in cancer patients only in countries such as Australia, Hong Kong, Ireland, and Turkey. It is done in cases of high ovarian hyperstimulation syndrome (OHSS) risk or to accumulate eggs for preimplantation genetic diagnosis (PGD) in Spain. Peru has been reported to have a bank of frozen donor oocytes. Vietnam and Austria are reported to resort to the procedure in cases of OHSS and failure to get the sperm sample. The respondent reported that Kazakhstan had started the practice since 2011.

Ovarian and testicular tissue were reported to have the possibility to be preserved under statute in 32 countries. There are guidelines reported to exist covering this subject in 36 countries. However, it was reported that this is not permitted in Ivory Coast and Senegal. It is practiced in 38 countries mainly for fertility preservation prior to cancer treatment. Uganda did not report any developed programs for the purpose, but in cases of malignancy, ovarian tissue freezing is done, if possible. In South Africa, it was reported that fertility preservation in malignancy cases is by the egg freezing method rather than ovarian tissue freezing; and in Argentina, the tissue freezing protocols are yet experimental.

## SUMMARY

Cryopreservation today is an essential facility in all ART programs. It is still being aggressively researched and long-term follow-up studies of children are required to allay safety concerns. As such, more specific regulations are needed and many countries are actively engaged in formulating these. The regulations could be in the form of laws, statutes, or guidelines.

Some agreement has been reached on the duration of the storage. There is moderate variation in the duration of storage of both fertilized eggs and oocytes. All ART programs and all donors of cryopreserved material must agree in writing on the disposition of any unused cryopreserved material.

Only a few countries prohibit the preservation of embryos, but allow the storage of oocytes. There are large numbers of frozen embryos in clinics, creating disposal issues, both legal and ethical. Family-breakdown has been followed by court disputes over ownership, so specific instructions for time-limited disposal should always be in place. Cryopreservation of oocytes may reduce these problems to a certain extent. There are some countries that allow offspring to be provided with identifying information regarding the gamete donor. This has led to reduction in donors. Furthermore, improving results with the ICSI technology has reduced the need for donor gametes. Donor oocyte cryopreservation is now better accepted and has helped improve the results of the technique. The time may now be right for replacing fresh with frozen donor oocyte cryopreservation program coupled with a 3 to 6 month quarantine period, to rule out the window period of viral infections, such as human immunodeficiency virus (HIV) 1 and 2.

The vapor-phase nitrogen system permits the storage of vitrified oocytes, maintaining their potential to develop into competent embryos in a manner similar to those oocytes stored in a standard liquid nitrogen system. This may prevent cross-contamination during the storage of vitrified samples (13). The storage of human semen in liquid nitrogen vapor, without direct contact with liquid nitrogen, may represent a useful alternative for the effective storage of human semen (14).

Comparing the methods of oocyte vitrification, the open and closed systems yielded similar freeze/thaw oocyte survival rates (15). Also, comparing development and DNA damage in cleavage- and blastocyst-stage embryos, vitrified by the open and closed systems, it was found that the closed carriers allowed sufficiently rapid temperature reduction to prevent DNA damage. Hence, given that the closed system reduces the possibility of tissue cross-contamination and has an equal performance, it may be preferable over the open system (16).

The results of methods for storage of testicular tissues are sparse, but it will be quite some time before more substantial data become available (17). The procedure of ovarian tissue cryopreservation has been found to be promising. There is good evidence of comparable congenital malformation rate as well as perinatal/child outcomes between fresh and frozen thawed cleavage-stage embryos, frozen by the slow freezing methods. A similar trend is seen after slow freezing of blastocysts and after vitrification of early cleavage-stage embryos, blastocysts, and oocytes. However, more long-term studies are necessary to validate these findings.

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| Table 6.1 Regulation of cryopreservation by statute | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| How ART is governed | Country | Cryopreservation of fertilized eggs allowed under statute | | Cryopreservation of oocytes allowed/used under statute | | | Cryopreservation of ovarian/testicular tissue allowed/used | | |
| | | Allowed | Not mentioned | Allowed | Not mentioned | Practiced | Allowed | Not mentioned | Practiced |
| By statutes | Belgium | + | | + | | | + | | + |
| | Bulgaria | + | | + | | | + | | + |
| | Colombia | + | | + | | | | + | + |
| | Croatia | + | | | Unknown | | + | | + |
| | Czech Republic | + | | + | | | + | | + |
| | Denmark | + | | + | | | + | | + |
| | Finland | + | | + | | | + | | + |
| | Greece | + | | + | | | + | | + |
| | Hungary | + | | | + | | | + | + |
| | Iceland | + | | + | | | | + | Not practiced |
| | Libya | + | | + | | | + | | + |
| | Portugal | | + | | + | | | + | Not mentioned |
| | Slovenia | + | | + | | | + | | + |
| | Tunisia | + | | + | | | | + | Not mentioned |

* Multiple replies submitted for the country but only one response included in table.

| Table 6.2 Regulation of cryopreservation by guidelines | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **How ART is governed** | **Country** | **Cryopreservation of fertilized eggs allowed** | | **Cryopreservation of oocytes allowed/ used under statute** | | | **Cryopreservation of ovarian/testicular tissue allowed/used** | | |
| | | **Allowed** | **Not mentioned** | **Allowed** | **Not mentioned** | **Practiced** | **Allowed** | **Not mentioned** | **Practiced** |
| By guidelines | Australia | + | | + | | | + | | + |
| | Cameroon | + | | | + | | + | | Not practiced |
| | Egypt | + | | + | | | + | | + |
| | India | + | | + | | | + | | + |
| | Ireland | + | | + | | | + | | + |
| | Ivory Coast | + | | + | | | Not allowed | | Not practiced |
| | Japan | + | | + | | | | + | + |
| | Philippines | + | | + | | | + | | + |
| | Singapore | + | | + | | | + | | + |
| | Vietnam | + | | + | | | | + | + |

* Multiple replies submitted for the country but only one response included in table.

| Table 6.3 Regulation of cryopreservation by statute and guidelines | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **How ART is governed** | **Country** | **Cryopreservation of fertilized eggs allowed** | | **Cryopreservation of oocytes allowed/used** | | | **Cryopreservation of ovarian/testicular tissue allowed/used** | | |
| | | **Allowed** | **Not mentioned** | **Allowed** | **Not mentioned** | **Practiced** | **Allowed** | **Not mentioned** | **Practiced** |
| Both statute and guidelines | Argentina | + | | + | | | + | | + |
| | Austria | + | | + | | | + | | + |
| | Belarus | + | | + | | | + | | + |
| | Brazil | + | | + | | | + | | + |
| | China | + | | + | | | + | | + |
| | France | + | | + | | | + | | + |
| | Hong Kong | + | | + | | | + | | + |
| | Israel | + | | + | | | + | | + |
| | Italy | + | | + | | | + | | + |
| | Kazakhstan | + | | + | | | + | | + |
| | Korea | + | | | + | | | + | + |
| | Latvia | + | | + | | | | + | + |
| | New Zealand | + | | + | | | + | | + |
| | Norway | + | | + | | | + | | + |
| | Russia | + | | + | | | + | | + |
| | South Africa | + | | | + | | + | | + |
| | Spain | + | | + | | | + | | + |
| | Sweden | + | | + | | | + | | + |
| | Switzerland | + | | + | | | + | | + |
| | Taiwan | + | | + | | | | + | Not mentioned |
| | Turkey | + | | + | | | + | | + |
| | United Kingdom | + | | + | | | + | | + |
| | United States | + | | + | | | + | | + |

* Multiple replies submitted for the country but only one response included in table.

| Table 6.4 No regulation of cryopreservation | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **How ART is governed** | **Country** | **Cryopreservation of fertilized eggs allowed** | | **Cryopreservation of oocytes allowed/used** | | | **Cryopreservation of ovarian/testicular tissue allowed/used** | | |
| | | **Allowed** | **Not mentioned** | **Allowed** | **Not mentioned** | **Practiced** | **Allowed** | **Not mentioned** | **Practiced** |
| None | Chile | | Unknown | | + | | + | | Not mentioned |
| | Democratic Republic of the Congo | | + | | Unknown | | | + | + |
| | Dominican Republic | + | | + | | | + | | + |
| | Ecuador | | + | | + | | | + | + |
| | Mexico | + | | | + | | | + | Not mentioned |
| | Panama | | + | | + | | | + | Unknown |
| | Peru | + | | + | | | + | | + |
| | Saudi Arabia | + | | + | | | + | | Unknown |
| | Senegal | + | | Not allowed | | | Not allowed | | Not practiced |
| | Togo | | + | | + | | | + | + |
| | Uruguay | + | | + | | | + | | + |
| | Venezuela | Not allowed | | + | | | + | | + |
| Unknown | Uganda | + | | + | | | + | | Unknown |

* Multiple replies submitted for the country but only one response included in table.

| Table 6.5 The duration of storage of cryopreserved fertilized eggs and respondents providing country-specific comments | | | |
|---|---|---|---|
| **How ART is governed** | **Country** | **Consensus on duration of storage of cryopreserved fertilized eggs** | **Comment on regulation of cryopreservation** |
| Statutes | | | |
| | Belgium | 5 years + extension allowed | Regulated by law |
| | Bulgaria | 5 years | Only those of good quality |
| | Colombia | No consensus | Clinical history of gamete donors, genetic test, psychological assessment, infectious disease tests, and previous quarantine |
| | Croatia | No consensus | |
| | Czech Republic | 12 years | Freezing is allowed for all of embryo development. |
| | Denmark | 5 years | In all clinics |
| | Finland | No limit | Routine in all IVF clinics |
| | Greece | - | |
| | Hungary | 5 years | |
| | Iceland | - | |
| | Libya | No consensus | Freeze with consent of husband and wife; the contract should be renewed yearly. |
| | Portugal | - | |
| | Slovenia | 5 years + extension of 5 years allowed | All viable, surplus embryos should be cryoconserved. |
| | Tunisia | 5 years + extension allowed | |
| Guidelines | | | |
| | Australia | 10 years | |
| | Cameroon | No consensus | |
| | Egypt | 5 years | |
| | India | 5 years + extension allowed | |
| | Ireland | No consensus | Offered by all clinics |
| | Ivory Coast | Not practiced | |
| | Japan | Unknown | Frozen embryos should be used during the marriage of the couple by the end of reproductive age of female |
| | Philippines | No consensus | Married couples, at least Grade 2+ cleavage-stage embryos |
| | Singapore | 5 years | |
| | Vietnam | Not practiced | |

| Table 6.5 The duration of storage of cryopreserved fertilized eggs and respondents providing country-specific comments (continued) | | | |
|---|---|---|---|
| **How ART is governed** | **Country** | **Consensus on duration of storage of cryopreserved fertilized eggs** | **Comment on regulation of cryopreservation** |
| Both statutes and guidelines | | | |
| | Argentina | 5 years | Informed consent of both partners, with annual renewals |
| | Austria | 10 years | Unlimited storage permitted |
| | Belarus | - | |
| | Brazil | No consensus | |
| | China | No consensus | Signed informed consent |
| | France | 5 years | Consent from the parents |
| | Hong Kong | 10 years for own gametes and anonymous donors' gametes; 2 years for designated donation of gametes | Married couples |
| | Israel | 5-10 years | Regulated by law |
| | Italy | No consensus | |
| | Kazakhstan | No limit | Ministry of Health instruction letter |
| | Korea | 5 years; above 5 years for cancer patients | |
| | Latvia | 10 years | |
| | New Zealand | 10 years + extension allowed | |
| | Norway | 5 years | |
| | Russia | No consensus | |
| | South Africa | No limit; but the law says that unclaimed embryos should be destroyed after 10 years. | Need consent to freeze them. If unclaimed for 10 years, they can be destroyed. |
| | Spain | Until menopause | |
| | Sweden | 5 years | For medical and social reasons |
| | Switzerland | 5 years | Only zygotes |
| | Taiwan | 10 years | |
| | Turkey | 5 years | |
| | United Kingdom | 10 years; unless exceptional circumstances. Transfer before age 50 of the female partner. | Couple consent |
| | United States | No limit; ASRM says that unclaimed embryos should be discarded after 10 years. | Used commonly in almost all programs. Success rates have increased dramatically with recent developments in vitrification technology. |

| Table 6.5 The duration of storage of cryopreserved fertilized eggs and respondents providing country-specific comments (continued) | | | |
|---|---|---|---|
| **How ART is governed** | **Country** | **Consensus on duration of storage of cryopreserved fertilized eggs** | **Comment on regulation of cryopreservation** |
| None | | | |
| | Chile | No consensus/no guidelines | |
| | Democratic Republic of the Congo | No consensus | No special requirements |
| | Dominican Republic | - | |
| | Ecuador | - | |
| | Mexico | No consensus | |
| | Panama | - | |
| | Peru | No limit | |
| | Saudi Arabia | No consensus | Consent of husband and wife |
| | Senegal | No consensus | |
| | Togo | No consensus | Supernumerary eggs |
| | Uruguay | No consensus | |
| | Venezuela | No consensus | Prezygotes to blastocysts |
| Unknown | | | |
| | Uganda | No consensus | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 7: Posthumous insemination

## INTRODUCTION

There are two common scenarios in which posthumous insemination (using sperm obtained prior to death or postmortem for IUI or ICSI procedure) may be performed:

1. The sperm was provided before the man's death with his written consent and/or a legal agreement detailing his wishes after death. For example, a man with cancer who cryopreserves his sperm before the start of chemotherapy and then subsequently dies.
2. Posthumous sperm retrieval (PSR) takes place after the death (or brain death) of a man without his prior written consent and/or legal agreement detailing his wishes.

In the first scenario, some countries allow the use of the dead man's sperm if his written consent has been obtained prior to his death. However, legislation in many countries only addresses the use of gametes/embryos in ART while the person is alive and may not specifically permit ART to be performed after a patient's death. The decision to proceed after death in these cases is usually made by a court of law, a physician, or hospital based on pre-existing consent forms and/or legal agreement. The inheritance rights of a future child may be an issue in these cases.

In the second scenario, where a man is either comatose (usually brain dead) or has just died (sperm may be harvested within 24 hours of his death), PSR may be performed. There is usually no written consent or legal agreement in place detailing his fertility wishes in the event that his spouse is widowed. The use of his sperm for ART in this scenario is very controversial and often banned by legislation or discouraged by ethical guidelines.

Orr and Siegler's journal article describes the ethical dilemmas related to the concerns about respect for the deceased individual, consent, the welfare of the child, and other legal issues related to posthumous sperm retrieval where no prior written consent exists (1). In this IFFS Surveillance survey, the term "posthumous insemination" may include both the above scenarios, and the results should be interpreted in this context.

## ANALYSIS OF SURVEY

There were valid responses to this survey from 73 respondents from 60 countries. The respondents were asked whether posthumous insemination was allowed in their country. The analyzed data showed that 25% replied that posthumous insemination was allowed. In 45% of the responses, it was not allowed, and in the remainder of the 25%, it was not mentioned in the legislation.

In the United Kingdom, Argentina, Australia, Greece, Hungary, Latvia, and New Zealand, respondents reported that posthumous insemination may only be done if there is written consent in place. In the United States, it is allowed in some states. In Israel, it was reported that a court order is necessary prior to performing the procedure.

The next question related to whether the procedure of posthumous insemination was actually used in the country surveyed. Thirty-three percent of the respondents indicated that it was used in their country, 43% said it was not used, and 24% replied that it was not known to them whether it was used or not. Table 7.1 shows the data by country.

## SUMMARY

Posthumous insemination is reported to be allowed in some countries, usually where prior written consent exists. Posthumous sperm retrieval after death without prior consent remains controversial; respondents stated that it is often not allowed by legislation and advised against in guidelines.

## REFERENCES

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| Table 7.1 Posthumous insemination | | | | |
|---|---|---|---|---|
| **Country** | **Allowed** | **Not allowed** | **Not mentioned in legislation** | **Used** |
| Argentina | + | | | + |
| Australia | + | | | + |
| Austria | | + | | |
| Belarus | | + | | |
| Belgium | + | | | + |
| Brazil | + | | | + |
| Bulgaria | | + | | |
| Cameroon | | + | | |
| China | | + | | |
| Chile | | | + | |
| Colombia | | | + | |
| Croatia | | | + | |
| Czech Republic | | + | | + |
| Democratic Republic of the Congo | | + | | |
| Denmark | + | | | |
| Dominican Republic | | | + | |
| Ecuador | | | + | |
| Egypt | | + | | |
| Finland | | + | | |
| France | | + | | |
| Greece | + | | | + |
| Hong Kong | | + | | |
| Hungary | | | + | + |
| Iceland | | | + | |
| India | + | | | |
| Ireland | | | + | + |
| Israel | | + | | + |
| Italy | | + | | |
| Ivory Coast | | + | | |
| Japan | | + | | |
| Kazakhstan | + | | | + |
| Korea | | + | | |
| Latvia | | | + | |
| Libya | | + | | |
| Mexico | | | + | |
| New Zealand | + | | | + |
| Norway | | + | | |
| Panama | | | + | |
| Peru | | + | | |
| Philippines | | | + | |
| Portugal | | | | |
| Russia | | | + | |
| Saudi Arabia | | | + | |
| Senegal | | + | | |
| Singapore | | + | | |
| Slovenia | | + | | |

| Table 7.1 Posthumous insemination (continued) | | | | |
|---|---|---|---|---|
| **Country** | **Allowed** | **Not allowed** | **Not mentioned in legislation** | **Used** |
| South Africa | | | + | |
| Spain | | | + | |
| Sweden | | + | | |
| Switzerland | | + | | |
| Taiwan | | + | | |
| Togo | | | + | |
| Tunisia | | + | | |
| Turkey | | + | | |
| Uganda | | | + | |
| United Kingdom | + | | | + |
| Uruguay | | + | | |
| United States | + | | | + |
| Venezuela | | + | | |
| Vietnam | + | | | + |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 8: Donation

## INTRODUCTION

Gamete and embryo donation are now widespread, established clinical practices in infertility therapy. However, there are considerable variations in their regional application, which is influenced by the legal, ethical, cultural, and religious traditions of their respective countries. Sperm banking and donation have been available for many years, for IVF and non-IVF applications, but oocyte banking has grown recently, with the advent of vitrification, a technique that is gradually replacing slow freezing. Recently, both ASRM and the European Society of Human Reproduction and Embryology (ESHRE) have endorsed oocyte freezing as a safe, standard procedure, capable of producing healthy babies. The technique currently is being used not only for oocyte donation, but also for those undergoing oncological treatment or other potential gonadotoxic therapies. It also is available for oocyte banking in women electing to postpone childbearing for personal or professional reasons. ESHRE's Task Force issued an updated document on the matter (1), and the latest ASRM Practice Committee opinion document states that "Evidence indicates that oocyte vitrification and warming should no longer be considered experimental" (2), changing the status of the previous document issued in 2008 (3). ASRM also has updated its Practice Committee Opinion on "Recommendations for Gamete and Embryo Donation," which replaces the 2008 document (4).

Almost 80% of the respondents said legislation regarding donation and anonymity of donors had not been modified since 2009 (data reported in the 2010 IFFS survey), although the positive responses (modifications in legislation) were only 8%, accounting mainly for European countries and Hong Kong.

## ANALYSIS OF THE SURVEY

### Countries with Statutes

This survey evaluated sperm donation (for IVF and non-IVF indications), egg donation, embryo donation, and germinal tissue (ovarian or testicular) donation and cryopreservation. Table 8.1 shows an overview of the situation in different countries, grouped by the way ART is governed. Legislation concerning sperm donation for IVF allows the procedure in 70% of countries, does not allow it in 10%, and does not mention it in 12%, and 8% of respondents stated that its status is unknown (Table 8.1). In countries reported to have statutes, various limitations and restrictions were verified, as is depicted in Table 8.2.

In Europe, sperm donation is used frequently, although different regulatory limitations were reported to be in place. Some countries were reported to allow only anonymous donation (Belarus, Bulgaria, Czech Republic, France, Hungary, Russia, Spain, and Switzerland). In others, only non-anonymous donation was reported to be allowed (Sweden and in Finland with limitations). In Sweden, sperm donation was reported to not be allowed in combination with egg donation. In the rest of the European countries with respondents who were surveyed, a combination of anonymous and non-anonymous donation situations were reported to exist, such as in Slovenia and Belgium. In Finland, it was reported that donors from abroad can be accepted but must be registered. Italy and Austria are the only European countries that were reported to not allow sperm donation for ART.

Screening and the enforcement of a quarantine period is reported as common practice in Europe and the United States and includes serologic testing, karyotyping, and cystic fibrosis genetic screening for

prospective parents. Some countries are reported to have specific limitations on the number of offspring produced (e.g., in Spain, 6; Latvia, 3; and Hungary, 3 successful pregnancies). In the United Kingdom, under The Human Fertilisation and Embryology Authority (HFEA) Code of Practice, sperm donation can be offered provided the donor is screened, agrees to release his identity on request of the recipient at 18 years old, and also limits the number of successful pregnancies achieved to 10. In Israel, it was reported that the law allows sperm donation for IVF.

In South Africa, the law was reported to relate specifically to screening and inclusion criteria for anonymous donors; in Australia, it was reported that donors and recipient couples are both obliged to receive counseling, and there is an "offspring limit" for sperm donation to a maximum of 10 families. China was reported to only allow sperm donation from public banks, and in Hong Kong, local authorities (Council on Reproductive Technologies) were reported to require traceable information from donors and limit donation to up to 3 offspring produced. In Korea, direct, open donation with the purpose of acquiring interests, money, or property was reported to be prohibited, and in India, it was reported that sperm donation can only be anonymous, screening is obligatory, and records have to be archived for 40 years. New Zealand and Kazakhstan law were reported to allow IVF sperm donation.

Respondents reported that sperm donation is not allowed in Egypt, Libya, Senegal, Tunisia, Saudi Arabia, and Turkey, and in other African countries it is not addressed (Uganda, Togo, Ivory Coast, and Democratic Republic of the Congo). In the majority of Latin America, respondents reported that it is not mentioned in laws or the status is unknown, with the exception of Brazil, Peru, and Uruguay, where it is reportedly legally permissible. Sperm donation is reported to be widely practiced in Argentina, Chile, Colombia, Ecuador, Dominican Republic, Mexico, Panama, and Uruguay, with screening standards in place that are similar to those in Europe and the United States. In Venezuela, it was reported that it is allowed in "specific cases."

In the case of donor sperm for use in non-IVF infertility, respondents stated that it is not allowed in 22% of the countries surveyed, it is permitted in 51% of the cases, it is not specifically mentioned in roughly 20% (suggesting that it is used in about 70% of countries), and the status is unknown in 4% (see Table 8.1).

Table 8.3 shows survey results on local or regional restrictions in donor sperm used for non-IVF treatments. In Europe, donor insemination programs are in place in the United Kingdom, Belarus, Belgium, Czech Republic, Denmark, Finland, France, Greece, Hungary, Latvia, Norway, Spain, Sweden, and Switzerland. Curiously, in Austria, it was reported that the law bans sperm donation for IVF, but it accepts it for non-IVF treatments. Other countries like Croatia, Iceland, Ireland, and Russia were reported to allow sperm donation for non-IVF treatments, but it is not explicitly addressed in their laws. Non-IVF sperm donation was reportedly not allowed in Bulgaria, Italy, and Slovenia (except for certain medical exceptions for the latter). Israel, as well as India and Kazakhstan, were reported to allow non-IVF sperm donation. In Hong Kong, it was reportedly accepted but providers must submit an application form to the National Council before initiating treatment. Respondents reported that the following countries do not allow donor sperm for non-IVF treatments: Australia, Cameroon, Democratic Republic of the Congo, Egypt, Libya, Saudi Arabia, Senegal, Tunisia, and Turkey. In Venezuela, it is reportedly only permitted under specific circumstances, and in China, reportedly only in cases of azoospermia during IVF is a couple allowed to use IUI with donor sperm. All Latin

American countries with respondents who were surveyed reported that they allow the use of donor sperm for non-IVF treatments.

More than half (53%) of the countries with respondents surveyed reported monetary compensation for sperm donors, while 31% did not report compensation, and 16% of the respondents did not know the status of donor compensation in their countries. In the majority of European countries, it was reported that donors receive compensation for expenses, costs, or transportation, ranging from 50 to 100 euros, on average. In the United States and Latin America, a similar situation was reportedly observed, with sperm banks establishing their own reimbursement criteria.

Respondents stated that egg donation is allowed by law in almost 70% of the countries (69.3%), not allowed in 12%, not mentioned in 16%, and the status is unknown in 4% of the countries (Table 8.1). Most European countries reportedly allow egg donation, with the exceptions of Austria, Italy, Norway, and Switzerland, although surprisingly, the latter two do permit sperm donation for IVF and non-IVF treatments. Slovenia was reported to allow egg donation in special cases.

Restrictions were reported to vary from country to country (Table 8.4); in the United Kingdom, it may be performed in accordance with the HFEA Code of Practice and donors must be screened and agree to provide their identity in the future on request. Oocyte sharing is also permitted. Most countries reportedly have established a mandatory age range for donors of 18-35 years old (Belarus, Czech Republic, Latvia, and Russia). In some cases, respondents stated that donors must have delivered a child previously (Belarus). Some countries reportedly only allow anonymous donation (Spain and France) or only non-anonymous (Finland and Sweden), or they establish a maximum number of offspring produced (Latvia, 3 and Spain, 6). Some countries allow family-related egg donation (Bulgaria and Hungary). Israel has reportedly a special law for oocyte donation, providing rules for donors and recipients and prohibiting trade for profit.

Respondents from China stated that egg donation is only permissible when an excess number of eggs (> 20) are retrieved from an IVF patient who has provided prior written approval. In Singapore, it was reported that it is only available to married couples, and in Korea, egg donors may undergo a maximum of 3 stimulated cycles. In India, only anonymous egg donation was reportedly accepted, and records have to be maintained for 40 years. Australia reportedly requires counseling for donors and recipients as with sperm donation, and respondents stated that South Africa allows egg donation under the aegis of guidelines provided by the National Health Act.

In Latin America, respondents referenced laws in Brazil and Colombia that permit anonymous egg donation after screening and also allow egg sharing.

**Countries with Guidelines**

Sperm donation for IVF is reportedly addressed in 76% of the countries governed by guidelines and not referred to in 14% of the cases. The practice of non-IVF sperm donation was reported as 47% of the countries, and 49% do not mention it in their guidelines. Overall, respondents surveyed from almost 80% of the countries report use of donor sperm for non-IVF infertility therapy, 16% report it is not used, and the status is unknown in 4%. Most of the countries were reportedly following guidelines developed by their scientific societies, ASRM or ESHRE, regarding serology, karyotyping, and cystic

fibrosis screening of donors (Table 8.6). Furthermore, reportedly, Argentina is developing an accreditation program for sperm banks.

With respect to egg donation, a similar trend is recognized from the survey, with 73% of the countries reportedly performing the procedure, 12% reporting it is "not mentioned" in the guidelines, and 14% not performing egg donation.

In most countries, screening is reportedly done for sexually transmitted diseases and cystic fibrosis (genetic testing for potential carriers). Also, donors are reported to have to be 18 to 35 years of age (Table 8.7). In Peru, it was reported that the age of the donor must not exceed 30. In Argentina, guidelines reportedly recommend additional screening for fragile X; donors there have to be between 21 and 34 years old with previous birth/s (recommended) and cannot exceed 6 donation cycles, and recipients must be less than 50 years of age. In Cameroon, recipients reportedly have to be a couple, and the recipient women must be below 50 years of age. In the United States, clinics follow voluntary ASRM guidelines for gamete donation.

Embryo donation to a patient or couple for reproductive purposes is reportedly allowed by law in 53% of countries, not allowed in 22%, not mentioned in 20% of the cases, and the status was unknown by the respondents in 4% (Table 8-5). A similar trend was noted in countries in which the practice is addressed by guidelines on embryo donation, with 55% reportedly allowing it, 26% prohibiting the practice, and 18% not addressing it. Embryo donation for stem cell research, on the contrary, was reportedly more extensively allowed, with 45% of the countries permitting it without restriction, an additional 20% allowing it with some restrictions and limitations, prohibition in 29%, and the status was unknown by the respondents in 6% of the countries.

**Countries with Statutes**

In countries with statutes and laws, embryo donation is allowed in the United Kingdom, as stipulated by the HFEA Code of Practice. It is also reportedly permitted in Belarus, Bulgaria, Czech Republic, and Latvia (if embryo is prospectively obtained with donated gametes from screened donors), Belgium (anonymous), Finland (registered gamete donors or registered couples), France (anonymous), Spain (anonymous from healthy couples), and Russia (from donated gametes or excess embryos from couples).

It is also reportedly allowed in South Africa, India (anonymously), Australia, New Zealand, Kazakhstan, and the United States, and in Latin American countries like Brazil, Colombia, Uruguay, and Venezuela ("specific cases"). In Singapore, it is reportedly only permitted in a couple with azoospermia and ovarian failure. In Israel, it is prohibited by law as well as in Austria, Denmark, Iceland, Italy, Norway, Slovenia, Sweden, and Switzerland, and the following countries: China, Egypt, Libya, Saudi Arabia, Senegal, Tunisia, and Turkey.

**Countries with Guidelines**

Informed consent from embryo donors and screening of donors is the main requisite in countries with guidelines, as in the United States (Table 8.8). In India, embryo donation is reportedly allowed in couples with gamete failure or genetic diseases. In New Zealand, case-by-case approval by an ethics panel is needed, and in Vietnam, an agreement between both parties is reportedly required. In Russia, embryos refused by IVF couples may be donated. In Argentina, a long-standing Court Appeal for

Protection issued against fertility centers has discouraged thawing embryos for donation and, subsequently, guidelines reviewed have not recommended embryo donation.

Donation of germinal tissue was also surveyed and 27% of respondents noted that the procedure is allowed. It is banned in 43% of countries, but its status was unknown by 30% of respondents. Most of the countries performing these procedures (Argentina, Brazil, Bulgaria, Czech Republic, Denmark, Greece, Hong Kong, Kazakhstan, Mexico, New Zealand, Slovenia, Spain, United Kingdom, United States, and Uruguay) responded that it was infrequently performed, usually in experimental protocols involving young cancer patients.

## SUMMARY

Gamete donation is an increasingly available therapeutic alternative, with sperm donation for IVF and non-IVF procedures and egg donation for IVF used by 70% of the countries surveyed. Different restrictions vary widely, but serological and genetic screening is reported to be widespread and consistent. Embryo donation is more frequently offered, although in some countries it is reportedly accepted only when the embryo is obtained from donor sperm and eggs. Germinal tissue donation is reported to be infrequently performed and is typically offered as an experimental procedure.

## REFERENCES

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3. Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. 2008 Guidelines for gamete and embryo donation: a Practice Committee report. Fertil Steril 2008;90 (Suppl 5):S30-44.
4. Recommendations for Gamete and Embryo donation: a Committee Opinion. Fertil Steril 2013; 99:47-62.

| Table 8.1 Gamete donation | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **How ART is governed** | **Sperm donation** | | | | | | | | **Oocyte donation** | | | **Embryo donation** | | |
| | **IVF** | | | **Non-IVF** | | | **Non-IVF use** | | | | | | | |
| ***Statutes/law*** | **A** | **NA** | **NM** | **A** | **NA** | **NM** | **Yes** | **No** | **A** | **NA** | **NM** | **A** | **NA** | **NM** |
| Australia | + | | | | + | | + | | + | | | + | | |
| Belgium | + | | | + | | | + | | + | | | + | | |
| Bulgaria | + | | | | + | | | + | + | | | + | | |
| Colombia | + | | | + | | | + | | + | | | + | | |
| Croatia | + | | | | | | | + | + | | | | | |
| Czech Republic | + | | | + | | | + | | + | | | + | | |
| Denmark | + | | | + | | | + | | + | | | | + | |
| Finland | + | | | + | | | + | | + | | | + | | |
| Hungary | + | | | + | | | + | | + | | | + | | |
| Iceland | + | | | | | + | | | + | | | | + | |
| Latvia | + | | | | + | | | + | + | | | + | | |
| Libya | | + | | | + | | | + | | | + | | | + |
| Slovenia | + | | | | + | | + | | + | | | | + | |
| Spain | + | | | + | | | + | | + | | | + | | |
| Greece | + | | | + | | | + | | + | | | + | | |
| Tunisia | | + | | | + | | | + | | + | | | + | |
| United Kingdom | + | | | + | | | + | | + | | | + | | |

**A: Allowed NA: Not allowed NM: Not mentioned**

| Table 8.1 Gamete donation (continued) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **How ART is governed** | **Sperm donation** | | | | | | | | **Oocyte donation** | | | **Embryo donation** | | |
| | **IVF** | | | **Non-IVF** | | | **Non-IVF use** | | | | | | | |
| ***Guidelines*** | **A** | **NA** | **NM** | **A** | **NA** | **NM** | **Yes** | **No** | **A** | **NA** | **NM** | **A** | **NA** | **NM** |
| Cameroon | + | | | | | + | + | | + | | | | | + |
| Egypt | | + | | | + | | | + | | + | | | + | |
| Hong Kong | + | | | | | + | + | | + | | | + | | |
| India | + | | | + | | + | + | | + | | | + | | |
| Ireland | + | | + | | | + | + | | + | | | | | + |
| Ivory Coast | | | + | | | + | | + | | + | | | | + |
| Philippines | | | + | | | | | | | | + | | | + |
| Singapore | + | | | + | | | + | | + | | | + | | |
| Vietnam | + | | | + | | | + | | + | | | + | | |

**A: Allowed NA: Not allowed NM: Not mentioned**

| Table 8.1 Gamete donation (continued) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **How art is governed** | **Sperm donation** | | | | | | | | **Oocyte donation** | | | **Embryo donation** | | |
| | **IVF** | | | **Non-IVF** | | | **Non-IVF use** | | | | | | | |
| **Both statutes and guidelines** | **A** | **NA** | **NM** | **A** | **NA** | **NM** | **Yes** | **No** | **A** | **NA** | **NM** | **A** | **NA** | **NM** |
| Argentina | + | | + | + | | + | + | | + | | + | | + | + |
| Austria | | + | | + | | | + | | | + | | | + | |
| Belarus | + | | | + | | | | | + | | | + | | |
| Brazil | + | | | + | | | + | | + | | | + | | |
| China | + | | | | + | | | + | + | | | | + | |
| France | + | | | + | | | + | | + | | | + | | |
| Hong Kong | + | | | + | | | + | | + | | | + | | |
| Israel | + | | | + | | | + | | + | | | | + | |
| Italy | | + | | | + | | | + | | + | | | + | |
| Kazakhstan | + | | | + | | | + | | + | | | + | | |
| Latvia | + | | | + | | | + | | + | | | | | + |
| New Zealand | + | | | + | | | + | | + | | | + | | |
| Norway | + | | | + | | | + | | | + | | | + | |
| Russia | + | | | + | | | + | | + | | | + | | |
| South Africa | + | | | + | | | + | | + | | | + | | |
| South Korea | + | | | | | + | + | | + | | | | | + |
| Sweden | + | | | + | | | + | | + | | | | + | |
| Switzerland | + | | | + | | | + | | | + | | | + | |
| Taiwan | + | | | + | | | + | | | | | | + | |
| Turkey | | + | | | + | | | + | | + | | | + | |
| United States | + | | | + | | | + | | + | | | + | | |

**A: Allowed NA: Not allowed NM: Not mentioned**

| Table 8.1 Gamete donation (continued) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **How art is governed** | **Sperm donation** | | | | | | | | **Oocyte donation** | | | **Embryo donation** | | |
| | **IVF** | | | **Non-IVF** | | | **Non-IVF use** | | | | | | | |
| ***Neither statutes nor guidelines*** | **A** | **NA** | **NM** | **A** | **NA** | **NM** | **Yes** | **No** | **A** | **NA** | **NM** | **A** | **NA** | **NM** |
| Chile | | | | | | | + | | | | + | | | + |
| Democratic Republic of the Congo | | | + | | + | | + | | | | + | | | + |
| Dominican Republic | | | | | | | + | | | | | | | |
| Ecuador | | | + | | | + | | | | | + | | | + |
| Libya | | + | | | + | | | + | | + | | | + | |
| Mexico | | | | + | | | + | | + | | | | | + |
| Panama | | | | | | | | | | | + | | | + |
| Peru | + | | | | | | + | | + | | | | | |
| Saudi Arabia | | + | | | + | | | + | | + | | | + | |
| Senegal | | + | | | + | | | + | | + | | | + | |
| Togo | | | + | | | + | + | | | | + | | | + |
| Uruguay | + | | | + | | | + | | + | | | + | | |
| Venezuela | + | | | | + | | + | | + | | | + | | |

**A: Allowed NA: Not allowed NM: Not mentioned**

* Multiple replies submitted for the country but only one response included in table.

| Table 8.2 Restrictions by IVF law on how donor sperm to be used; survey respondent comments | |
|---|---|
| **Country** | **Comments** |
| Australia | Donors and recipients to have counseling. Maximum donation to 10 families. |
| Belarus | Anonymous, testing, and 6-month quarantine period |
| Belgium | Principle of anonymity, but known donation is allowed |
| Brazil | Anonymous, testing, and quarantine requirements |
| Bulgaria | Anonymous, testing, and quarantine requirements |
| Cameroon | Facilities, equipment, qualified staff |
| China | Sperm samples only from national sperm bank, no private banks |
| Colombia | Testing standards for genetic and infectious diseases, and previous quarantine |
| Czech Republic | Anonymous, 18 to 40 years, no genetic abnormality in family history, normal karyotyping, negative cystic fibrosis, negative sexually transmitted disease |
| Finland | Registered donors (also possible from abroad) |
| France | Anonymous |
| Hong Kong | Open donor or designated donor only, must be able to supply traceable information, applying to the Council on Human Reproductive Technology<br>Testing similar to European Union standards. |
| Hungary | Anonymous, maximum 35 years old, negative human immunodeficiency virus (HIV) 1-2, hepatitis B virus surface antigen (HbsAg), hepatitis C virus (HCV), and normal psychological tests. Maximum donation 3 successful pregnancies. |
| India | Testing standards. Donor identity cannot be revealed to patients and patient identity cannot be revealed to donor. Records have to be maintained for 40 years. |
| Israel | Healthy males, testing standards |
| Kazakhstan | If needed, with letter to Ministry of Health |
| Latvia | Healthy male, 18-45 years old, not more than 3 live-born children allowed in one country. |
| Russian Federation | Anonymous, 18-35 years old, testing, and positive conclusion from geneticist and psychologist |
| Slovenia | Anonymous preferred |
| South Africa | The law governs the use of anonymous donor sperm in detail, including screening and inclusion. |
| South Korea | Donations for the purpose of acquiring interests in money or property or other considerations is prohibited. |
| Spain | Anonymous, not more than 6 pregnancies |
| Sweden | Not in combination with egg donation, donors must be non-anonymous |
| Switzerland | Anonymity of the donor until the child's majority. The child is the only person who can request to know the donor identity. |
| United Kingdom | Welfare of the child assessment carried out, testing, and agreement for identity to be released to any donor-conceived people once they are 18 years old. Maximum 10 successful pregnancies |
| Venezuela | Specific cases |
| Vietnam | Agreement between donor and recipient |

* Multiple replies submitted for the country but only one response included in table.

| Table 8.3 Restrictions by law on how donor sperm in non-IVF infertility to be used; survey respondent comments | |
|---|---|
| **Country** | **Comments** |
| Austria | Several requirements and regulations |
| Belarus | Anonymous, testing, and quarantine requirements |
| Belgium | Implementation of EU cell and tissue directive into Belgian law |
| Brazil | Anonymous, testing, and quarantine requirements |
| Chile | There is no regulation for third-party reproduction. |
| China | Only allowed if azoospermia is verified during IVF |
| Czech Republic | Same as in IVF |
| Democratic Republic of the Congo | Many donors are family members. It is required for insemination. |
| Finland | Registered donors |
| France | Anonymous |
| Greece | Anonymous, informed consent, only reimbursement of expenses and medical costs up to 300 euros |
| Hong Kong | Same as in IVF |
| Hungary | Same as in IVF |
| India | Same as in IVF |
| Israel | Same as in IVF |
| Italy | Gamete and embryo donation is not allowed in Italy. |
| Kazakhstan | Same as in IVF |
| Latvia | Same as in IVF |
| Slovenia | Only allowed for strict medical indication |
| South Africa | There are regulations pertaining to the use of donor sperm in the National Health Act. |
| Spain | Same as in IVF |
| Sweden | Donors must be non-anonymous. |
| Switzerland | Donor sperm insemination can be used in married couples. |
| United Kingdom | Same as in IVF |

* Multiple replies submitted for the country but only one response included in table.

| Table 8.4 Special requirements if the law allows donor eggs to be used in IVF; survey respondent comments | |
|---|---|
| **Country** | **Comments** |
| Australia | Age, maternity, consanguinity; counseling for donors and recipients |
| Belarus | Younger than 35, donor should have a child |
| Belgium | Principle of anonymity, but known donation is allowed |
| Brazil | Anonymous, testing, women can share the costs |
| Bulgaria | Mainly anonymous, except cases of sisters or close relative donation |
| China | Only when oocytes retrieved > 20, and patients agree |
| Colombia | Testing standards for genetic and infectious diseases, psychological counseling |
| Czech Republic | 18 to 35 years, no genetic abnormality in family history and normal karyotyping, negative cystic fibrosis, negative sexually transmitted diseases |
| Finland | Registered donors |
| France | Anonymous |
| Greece | Anonymous, reimbursement of 1,400 euros |
| Hong Kong | Anonymous and designated egg donors allowed. Follow ASRM guidelines. Application to the Council on Human Reproductive Technology. |
| Hungary | Anonymous donation in institutes, nominated donation allowed only between close relatives |
| India | Donor screening; anonymous, identity cannot be revealed. Records have to be kept for 40 years. |
| Israel | Special law with details |
| Kazakhstan | Instruction letter to the Ministry of Health |
| Latvia | Healthy female aged 18-35, not more than 3 live-born children per country. |
| Russian Federation | Age 18-35, testing and positive conclusion from geneticist and psychologist |
| Singapore | Only married couples |
| Slovenia | Only under strict medical indication |
| South Africa | Governed by the National Health Act. Donors > 18 years old, no medical, family history, genetic conditions, or mental problems |
| South Korea | Up to 3 cycles, at least every 6 or more months, expenses can be paid |
| Spain | Anonymous, not more than 6 pregnancies |
| Sweden | Non-anonymous, health screening |
| United Kingdom | Testing in accordance with HFEA Code of Practice, egg sharing allowed; agreement for identity to be released to any donor-conceived people once they are 18 years old. Maximum £750 compensation |
| Venezuela | Done in specific cases |
| Vietnam | Agreement between donor and recipient |

* Multiple replies submitted for the country but only one response included in table.

| Table 8.5 Special requirements if the law allows embryo donation; survey respondent comments | |
|---|---|
| **Country** | **Comments** |
| Australia | Counseling for both partners, screening |
| Belarus | Donor embryo = donor egg + donor sperm |
| Belgium | Anonymous |
| Brazil | Anonymous, serology testing |
| Bulgaria | Donor embryo = donor egg + donor sperm |
| Colombia | Testing standards for genetic and infectious diseases, psychological counseling |
| Czech Republic | Healthy donors complying standards for egg donation + sperm donation |
| Finland | Registered donors (embryos, or oocyte + sperm) |
| France | Anonymous |
| Hong Kong | Anonymous donor <35 and free from infectious diseases, designated donor also; application to be made to the Council on Human Reproductive Technology |
| Hungary | Anonymous donation in institutes, nominated donation only between close relatives |
| Kazakhstan | Instruction letter to the Ministry of Health |
| Latvia | Donor embryo = donor egg + donor sperm |
| New Zealand | One recipient couple per donor couple; case by case approval by ethics committee |
| Russian Federation | Embryo from donor's egg and sperm or any embryo refused by patients after IVF treatment |
| Singapore | Only to recipient couples with azoospermia + ovarian failure |
| South Africa | Consent from the original couple needed |
| Spain | Anonymous and belonging to healthy couples |
| Greece | Anonymous and belonging to healthy couples |
| United Kingdom | In accordance with HFEA Code of Practice, agreement for identity to be released to any donor-conceived people once they are 18 years old |
| Venezuela | Done in specific cases |
| Vietnam | Agreement between donor and recipient |

* Multiple replies submitted for the country but only one response included in table.

| Table 8.6 Restrictions in guidelines to donor sperm used in IVF; survey respondent comments | |
|---|---|
| **Country** | **Comments** |
| Argentina | Inclusion criteria, serology and genetic screening. Argentine Society of Reproductive Medicine (SAMeR) is working currently on new guidelines for sperm bank accreditation, ethics code of practice in place |
| Belarus | Donor must be < 40 years old, should have a child |
| Cameroon | Approved center with staff and equipment suitable |
| India | Donor sperm is allowed in nonobstructive azoospermia, if husband is carrier of a hereditary genetic defect, if husband has severe oligozoospermia, and couple does not want ICSI. |
| New Zealand | Ethics approval for cross-generational donation |
| Peru | Anonymous, serology and genetic screening |
| Singapore | Only married couples |
| United States | Follow ASRM guidelines |

* Multiple replies submitted for the country but only one response included in table.

| Table 8.7 Restrictions in guidelines for egg donation; survey respondent comments | |
|---|---|
| **Country** | **Comments** |
| Argentina | Serology and genetic screening, including fragile X, maximum number of cycles recommended and compensation. Recipient up to 50 years old. |
| Cameroon | Recipient age less than 50. Couple needed. |
| India | Donor from age 18 to 35 years old, screened for sexually transmitted diseases, karyotyping, and hemoglobin electrophoresis. |
| Kazakhstan | Age, health, not less than 1 child in the family |
| New Zealand | Ethics approval for cross-generational donation |
| Peru | Donors must be under 30 years old, serologic, toxicological and genetic screening |
| Singapore | Married couples |
| United States | Follow ASRM guidelines for gamete donation |

* Multiple replies submitted for the country but only one response included in table.

| Table 8.8 Special requirements if guidelines allow donor embryos; survey respondent comments | |
|---|---|
| **Country** | **Comments** |
| Argentina | Signed informed consent from the original parents. Procedure discouraged after a Court Appeal for Protection of the cryopreserved embryos in some clinics |
| Australia | Counseling for both parts |
| Bulgaria | Only if embryos are obtained from anonymous donor oocyte and sperm |
| India | In cases of primary germ failure and in inheritable genetic disorders |
| Kazakhstan | Letter to the Ministry of Health |
| New Zealand | Case by case approval by ethics committee |
| Peru | Documentation with a lawyer |
| Russia | Embryo from donor's egg and sperm or any embryo refused by patients after IVF treatment |
| Singapore | Only to married couples |
| South Africa | If patients consent to donate their embryos to another infertile couple |
| Spain | Embryo donation has to be anonymous |
| Venezuela | In specific cases |
| Vietnam | Agreement between donor and recipient |
| United States | Screening and informed consent from donors |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 9: Anonymity

## INTRODUCTION

Anonymous gamete donation has been standard practice since its inception in assisted reproduction. However, recently some countries have embraced a more open and transparent model in which non-identifying and identifying data from prospective donors are registered and preserved so that they may be released to the offspring at some point in the future (1,2). The psychological needs and civil rights of people conceived through gamete donation have received greater consideration, reflected by a growing literature and existing ASRM guidelines (3).

## ANALYSIS OF THE SURVEY

Modifications in legislation on anonymity were reported by 8% of the respondents, mainly in some European countries (Table 9.1). In the United Kingdom, anonymous donors who donated prior to April 1, 2005 can now be contacted and offered the option of now being re-registered as non-anonymous (4). In Denmark, it was reported that legislation now allows non-anonymous gamete donation, as is the case in Russia and Belarus (although Belarus only permits anonymous donation with cryopreserved, quarantined gametes after 6 months). Portugal has established a public national gamete bank, and in Hong Kong, it was reported that sperm donation is allowed openly (anonymous and non-anonymous donation), but egg donation must be designated (non-anonymous). In the United Kingdom and Switzerland, offspring have the right to request that the identity of the donor be divulged at age 18.

Disclosure of information on the donor to the offspring is enforced by statute in 20%-36% of the countries based upon the respondents surveyed, although approximately 30% of countries had respondents who report that they do not address disclosure in their legislation. The status was unknown, based upon the feedback provided from respondents in 6%-8% of the countries. When queried regarding use of "identifying" and "non-identifying" information on donors, law more commonly required non-identifying information; approximately 36% versus 24% requested "identifying information." When analyzing this issue in the countries that have guidelines, the same trend was verified, with guidelines reported as being most commonly suggesting "non-identifying information" (34%) over "identifying information" (22%), although in 24%-26% of the cases, identifying or non-identifying information is "not mentioned" in those guidelines. Roughly, 38% of the countries with guidelines on this issue were reported as not permitting identifying information on the donor to be disclosed. Table 9.2 summarizes the respondents' feedback depicting different methods employed by various countries in which the status of anonymity is addressed with regard to offspring.

### Countries with Statutes/Law

Based upon the results from our respondents, in the United Kingdom, the law allows offspring to be provided on request with non-identifying information about the donor from the age of 16 and with identifying information when they are 18 years old. In Austria, respondents stated that offspring can request non-identifying data at any age and identifying data after 14 years old. In Switzerland, respondents state that only identifying data can be provided at 18 years of age. Respondents also state that in Belgium, both non-identifying and identifying data can be revealed, but the latter only when there has been a previous formal agreement; Belarus, Bulgaria, Slovenia, and Israel do not allow disclosure of data from donors; and the Czech Republic, Greece, Hungary, and Latvia only disclose non-identifying information, as is the case in India and South Africa. Furthermore, respondents from Spain stated that identifying information will only be disclosed if a serious illness appears in the offspring, and France only allows use

of non-identifying data if a special commission accepts it. Respondents also state that in Denmark, Finland, Iceland, Kazakhstan, and Sweden, both identifying and non-identifying data have to be disclosed on request at 18 years of age, and in Sweden it is mandatory. In Australia and New Zealand, both identifying and non-identifying data can be requested at 18 years, and donors have to consent before participation. In the United States, offspring are generally not given identifying information, but guidelines recommend that non-identifying information be provided. Respondents have noted that Brazil allows non-identifying information disclosure, while in Colombia it is not addressed by current guidelines or statutes. In China, the survey revealed that only non-identifying information from sperm donors can be requested.

### Countries with Guidelines

Furthermore, the respondents reported that in India, information can be provided only following court order. In Japan, The Obstetrics & Gynecological Society guidelines recommend anonymous donation but suggest keeping records. The Argentinian Society recommends the same practice, although giving information about donors is not mandatory and remains controversial. Respondents have noted that in other Latin American countries, national guidelines do not address the issue of anonymity, and in the United States, respondents report that the preferences of patients and other involved parties are often followed.

## SUMMARY

Current practices regarding enforcement of anonymity and disclosure of information to the offspring and parents about gamete and embryo donation are evolving, and the trend is shifting away from exclusively anonymous donation to one with considerably more flexibility and openness.

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3. Informing offspring of their conception by gamete donation. Fertil Steril 2004 81 (3):528-531.
4. HFEA Code of Practice. http://www.hfea.gov.uk/333.htmlhttp://www.hfea.gov.uk/333.html

| Table 9.1 Modifications to anonymity | |
|---|---|
| **Country** | **Main modifications reported** |
| Belarus | Non-anonymous donation now possible (only with 6-month quarantine) |
| Belgium | Identifying information on the donor is now legal although not implemented yet |
| Denmark | Non-anonymous donation now possible |
| Hong Kong | Sperm donation now can be anonymous and non-anonymous; egg donation only non-anonymous |
| Portugal | Public gamete bank opened |
| Russia | Non-anonymous donation now possible |
| Switzerland | Offspring now allowed to request donor identity at 18 years old |
| United Kingdom | Previous anonymous donors (conceptions previous to April 1, 2005) can now be contacted and offered to be re-registered as non-anonymous. Offspring now allowed to request donor identity at 18 years old. |

* Multiple replies submitted for the country but only one response included in table.

| Table 9.2 Anonymity | | | | | | |
|---|---|---|---|---|---|---|
| **How ART is governed** | **Offspring provided on request with donor identifying information** | | | **Offspring provided on request with donor non-identifying information** | | |
| ***Statutes/law*** | **Yes** | **No** | **Not mentioned** | **Yes** | **No** | **Not mentioned** |
| Australia | + | | | + | | |
| Austria | + | | | + | | |
| Belgium | + | | | + | | |
| Belarus | | + | | | + | |
| Bulgaria | | + | | | + | |
| Colombia | | | + | | | + |
| Croatia | | | + | | | + |
| Czech Republic | | + | | + | | |
| Denmark | + | | | + | | |
| Finland | + | | | + | | |
| France | | + | | + | | |
| Greece | | + | | + | | |
| Hungary | | + | | + | | |
| Iceland | + | | | + | | |
| Israel | | + | | | + | |
| Kazakhstan | + | | | + | | |
| Latvia | | + | | + | | |
| New Zealand | + | | | + | | |
| Slovenia | | + | | | + | |
| South Africa | | + | | + | | |
| Spain | | + | | + | | |
| Sweden | + | | | + | | |
| Switzerland | + | | | | + | |
| United Kingdom | + | | | + | | |
| ***Guidelines*** | **Yes** | **No** | **Not mentioned** | **Yes** | **No** | **Not mentioned** |
| Cameroon | | | + | | | + |
| Egypt | | | + | | | + |
| India | | + | | + | | |
| Ireland | | | + | | | + |
| Ivory Coast | | + | | + | | |
| Japan | | + | | | + | |
| Philippines | | | + | | | + |
| Singapore | | + | | | + | |
| Vietnam | | + | | + | | |

| Table 9.2 Anonymity (continued) | | | | | | |
|---|---|---|---|---|---|---|
| **How ART is governed** | **Offspring provided on request with donor identifying information** | | | **Offspring provided on request with donor non-identifying information** | | |
| ***Both statutes and guidelines*** | **Yes** | **No** | **Not mentioned** | **Yes** | **No** | **Not mentioned** |
| Argentina | | | + | + | | |
| Brazil | | + | | + | | |
| China | | + | | + | | |
| Hong Kong | | + | | + | | |
| Israel | | + | | + | | |
| Italy | | + | | | + | |
| Kazakhstan | + | | | + | | |
| Latvia | | + | | + | | |
| New Zealand | + | | | + | | |
| Norway | + | | | | | + |
| Russia | + | | | + | | |
| South Africa | | + | | + | | |
| South Korea | | | + | | | + |
| Taiwan | | + | | | | + |
| Turkey | | | + | | | + |
| United States | | | + | + | | |
| ***Neither statutes nor guidelines*** | **Yes** | **No** | **Not mentioned** | **Yes** | **No** | **Not mentioned** |
| Chile | | | + | | | + |
| Democratic Republic of the Congo | | | + | | | + |
| Dominican Republic | | | + | | | + |
| Ecuador | | | + | | | + |
| Libya | | | + | | | + |
| Mexico | | | + | | | + |
| Panama | | | + | | | + |
| Peru | | + | | | | + |
| Saudi Arabia | | + | | | + | |
| Senegal | | + | | | + | |
| Togo | | | + | | | + |

| Table 9.2 Anonymity (continued) | | | | | | |
|---|---|---|---|---|---|---|
| **How ART is governed** | **Offspring provided on request with donor identifying information** | | | **Offspring provided on request with donor non-identifying information** | | |
| ***Neither statutes nor guidelines*** | **Yes** | **No** | **Not mentioned** | **Yes** | **No** | **Not mentioned** |
| Uruguay | | + | | | + | |
| Venezuela | | + | | | + | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 10: Micromanipulation

## INTRODUCTION

Micromanipulation techniques in ART are designed to increase the chances of a successful IVF cycle.

### *Microinsemination or intracytoplasmic sperm injection (ICSI)*

Fertilization of the oocyte is technologically the core of IVF. Attempts to perfect this fertilization process, in the presence of impaired sperm function, led to a series of micromanipulation techniques, from zona drilling, zona cracking, zona softening, partial zona dissection, and subzonal sperm injection, to the now routinely performed and well-established technique of intracytoplasmic sperm injection. In cases of azoospermia, ICSI is done using surgically retrieved sperm, obtained either from the epididymis (MESA or PESA) or the testis (TESA or TESE/micro-TESE). In such cases, as long as a viable spermatozoon is isolated, there is a fair chance of achieving a pregnancy. The fertilization and pregnancy rates achieved with surgically retrieved specimens match those seen with optimal male gametes (1). The clinical pregnancy rate is higher in obstructive azoospermia rather than in nonobstructive azoospermia (2). In cryptozoospermia (the constant presence of isolated sperm cells in the ejaculate that can be found after an extended microscopic search, as per the World Health Organization [WHO] laboratory guideline), testicular sperm extraction is justified in patients who fail to conceive by ICSI using ejaculated spermatozoa, as it offers higher pregnancy rates (3). Surgically retrieved sperm can be cryopreserved for future use.

There are no data to support the routine use of ICSI for non-male factor infertility. ICSI also may be beneficial for patients using preimplantation genetic testing, *in vitro* maturation (IVM), or cryopreserved oocytes (4). The association of severely impaired spermatogenesis and a high frequency of Y-chromosomal microdeletions as well as other karyotype anomalies have raised concerns regarding the genetic defects that can be transmitted to the offspring. Hence, genetic evaluation of the male with impaired spermatogenesis is preferably done before ICSI. Other than the ART-related higher incidence of multiple gestations with its associated neonatal risks, the health of ART offspring seems comparable to those spontaneously conceived, even considering the older age of the female partners. Children conceived through ART are at an increased risk of congenital malformations. Whether ICSI offspring have an added risk compared with IVF children is unclear. The risk of congenital anomalies seems to be lower in the more recent generations of ART children as compared with children born from older ART practices (5).

### *Assisted hatching (AH)*

Assisted hatching involves artificial disruption of the zona pellucida as a therapeutic option to improve the capacity of the embryos to implant. A variety of AH techniques have been employed including zona thinning, zona drilling and complete removal of the zona, use of chemicals, other mechanical techniques, and the use of the presently well-established technique of non-contact diode lasers. In the past decade, AH has been offered to patients with frozen-thawed embryos or patients who have suffered recurrent IVF-ET failure, with good outcomes. AH does not improve clinical pregnancy rates when performed in fresh embryos transferred to unselected or non-poor prognosis women or to women of advanced age (6). Recent studies have shown a slight increase in clinical pregnancy rates, just reaching statistical significance (7). AH also is used to open the zona pellucida of the embryo prior to PGD.

***Cytoplasmic transfer***

Cytoplasmic transfer between oocytes, initially developed to treat infertile patients who exhibited persistent poor embryonic development and recurrent implantation failure after IVF, was based on the assumption that the ooplasm of eggs of older women was defective and could be rescued by the introduction of ooplasm from eggs of younger donors. The procedure increased cleavage rates of the recipient embryos compared with non-injected controls, suggesting the presence of a factor from the ooplasm capable of rescuing a developmental block. The beneficial effects are believed to be derived from the mitochondrial component of the injected cytoplasm. Children born as a result of this technique have demonstrated heteroplasmy, the presence of two different strains of mitochondrial DNA in their genome (8). Because of the introduction of third-party DNA, cytoplasmic transfer has been reported to be prohibited in several countries.

## ANALYSIS OF THE SURVEY

ART legislation and guidelines are being constantly updated and modified in countries all over the world. There have been such modifications reported by respondents in 22 of the 60 countries, and respondents from 17 of these countries considered these to be an improvement. Micromanipulation practices in 14 countries are reported as being governed by statute, conducted within guidelines in a further 10 countries, and under both statutes and guidelines in 23 countries (Table 10.1). There are neither laws nor guidelines reported to exist on this issue in 12 countries. Uganda is one country where the respondent reported that the status of the regulation of micromanipulation is unknown.

Among all respondents who provided feedback for the survey, ICSI seems to be an accepted clinical practice. In no country was it reported that it is prohibited by statute or guidelines. It was reported to be specifically allowed in the statutes of 12 countries and in the guidelines of 9 others. Respondents stated that in those governed by both statutes and guidelines, it is permitted in 20 of the 23 countries; in all others, it is not mentioned; and it is practiced without restrictions in all countries, including the 11 countries that have neither statutes nor guidelines. Togo is reported to be the only country with no known ART governance, where its status on this issue is unknown by the respondent. In Brazil, respondents state that ICSI is almost always used for all ART cycles. Also in Australia, Ireland, Finland, Libya, and the United States, it is reported to be routinely employed in some units. In South Africa and Slovenia, 50%-60% of the ART cycles, respondents state, are using ICSI technology. In Venezuela, it was reported to be used for specific cases only.

Assisted hatching, with the exception of Ivory Coast and Senegal, was also reported to be a generally accepted procedure in the other 58 countries. It is reported by the respondents that AH is specifically allowed in 11 of the countries with statutes, and in 7 of the 10 countries with guidelines. In those governed by both statutes and guidelines, the respondents claim that it is permitted in 14 of the 23 countries. In the remaining countries, the respondents reported that its status is unknown. In the United States, assisted hatching is very commonly used for women over age 38, cryopreserved/thawed embryos, and thick zona pellucida, or for women with repeated implantation failure. Respondents claim that in Austria, several programs offer the technology; in China and Venezuela, it is used for specific cases only; and in South Africa and Spain, it was used more in the past than it is at present. The respondent from Libya reported that the technique is considered for use only if indicated by specified inclusion criteria. Respondents from Belgium, Denmark, and Latvia reported that there are only a few clinics using the technology. In Italy, the technique is reported to be used in very few cases and the national registry does not specifically require data regarding it. Respondents from the Czech Republic and Israel seldom use assisted hatching.

The respondents from Uganda stated that there are no specific guidelines yet, and their status regarding the practice of assisted hatching was unknown. The use of AH is permitted in Finland and Sweden, but it is reported to be infrequently used. It is permitted in Cameroon, but the respondent claimed it is not in use because of lack of equipment. It is not used in Croatia, Democratic Republic of the Congo, Peru, and Slovenia, according to the respondents from these countries.

Cytoplasmic transfer was reported to be used infrequently throughout the world and to be permitted only in the following 5 countries: Argentina, Greece, India, Kazakhstan, and the United Kingdom. Its use is reported to not be allowed in 25 countries, including 3 (of 14) with statutes, 3 (of 10) with guidelines, and 15 (of the 23) governed by both statutes and guidelines. In addition, it was reported as not being used in 4 (of 12) countries that have neither statutes nor guidelines.

In the United States, cytoplasmic transfer and cloning are prohibited by law through a US Food & Drug Administration (FDA) letter stating that use of any such technology must be approved by them; to date, they have not approved any applications. Respondents have reported that in France, only approved research programs have permission to use cytoplasmic transfer; in Austria, it is forbidden by law and not mentioned in the guidelines; and in the United Kingdom, consultations are ongoing regarding mitochondrial replacement by cytoplasmic transfer.

| **All comments provided by the respondents** | |
|---|---|
| **Under statute. ICSI** | |
| Colombia | The law does not mention the techniques to be implemented in this process. |
| Czech Republic | No limits for ICSI |
| Finland | Routine practice |
| Libya | Freely allowed for married couples. Has replaced the IVF procedure >90% |
| Slovenia | 50% of IVF |
| **Under statute. Assisted hatching** | |
| Belgium | Practiced by only a few programs |
| Croatia | Not practiced |
| Czech Republic | Not much used at this time |
| Denmark | Used in a few clinics only |
| Finland | AH is allowed but is not practiced, or probably very little (in some private clinics only) |
| Libya | Used in indicated cases |
| Tunisia | Not practiced. |
| **Under statute. Other types of micromanipulation such as cytoplasmic transfer** | |

| | |
|---|---|
| Greece | Law, under conditions and after approval by the Authority, allows experimentation in gametes and embryos. |
| **Under guidelines. ICSI** | |
| Australia | Routine treatment by some units. |
| India | ICSI is done in cases of severe male factor infertility, fertilization failures with standard IVF treatment, or if the numbers of spermatozoa are too low in the ejaculate. |
| Ireland | Widely used |
| **Under guidelines. Assisted hatching** | |
| Cameroon | AH is not practiced because of lack of equipment, but the technique is not forbidden as such. |
| Ivory Coast | Not allowed and not practiced |
| **Under both statutes and guidelines. ICSI** | |
| Austria | Not mentioned in the law, not mentioned in any guideline. Allowed without restrictions. |
| Brazil | Almost 100% of "IVF" cycles |
| China | ICSI is used for male infertility. |
| Latvia | Guidelines are under preparation, but the procedure is being practiced. |
| South Africa | There is a high ICSI rate in the private clinics, practiced in >60% of cases for *in vitro* fertilization. |
| Sweden | Regulated by law |
| United Kingdom | ICSI is practiced in accordance with HFEA Code of Practice. |
| United States | No limitations to the use of ICSI and it is used everywhere frequently |
| **Under both statutes and guidelines. Assisted hatching** | |
| Austria | Several programs offer AH |
| China | Practiced in cases of indications, according to patient's history and embryo assessment |
| Israel | Seldom used |
| Italy | This technique is used in very few cases, and the national registry does not specifically request data about it. |
| Latvia | Guidelines are under preparation, but the procedure is being practiced at some clinics. |
| South Africa | Very rarely performed now, but some clinics still do use the technology |
| Spain | Was used in the past |
| Sweden | AH is allowed but is not practiced any more, other than exceptionally. |
| United Kingdom | Practiced in accordance with HFEA Code of Practice |

| | |
|---|---|
| United States | Very commonly used for women over age 38, cryopreserved/ thawed embryos, thick zona pellucida, or for women with repeated implantation failure |
| **Under both statutes and guidelines. Other types of micromanipulation such as cytoplasmic transfer** | |
| Argentina | Not used. Some techniques, MACS,certain sperm selection devices, and motile sperm organelle morphology examination (MSOME) ICSI, are mentioned as experimental. |
| Austria | Not used. Forbidden by law, not mentioned in the guidelines |
| China | Not used. Cytoplasmic transfer is prohibited. |
| France | Used only by approved research programs |
| Kazakhstan | Allowed and used as per Ministry of Health instruction letter |
| South Africa | Not used. These technologies are excluded as per the National Health Act law. |
| United Kingdom | Not used. Consultations are in place regarding cytoplasmic transfer and mitochondrial replacement use for the future. |
| United States | Not used. Cytoplasmic transfer and cloning are prohibited by law through an FDA letter stating that use of any such technology must be approved by them, but they have not approved any use of it. |
| **Under neither statutes nor guidelines. ICSI** | |
| Democratic Republic of the Congo | ICSI is practiced without special conditions. |
| Dominican Republic | |
| Togo | ICSI is not practiced. |
| Venezuela | Used in specific cases only |
| **Under neither statutes nor guidelines. Assisted hatching** | |
| Democratic Republic of the Congo | Not practiced |
| Peru | AH is not used as such, but is used to do a trophoblast biopsy on day 5 of fertilization. |
| Senegal | Not allowed and not practiced |
| Venezuela | Used in specific cases only |
| **Under neither statutes nor guidelines. Other types of micromanipulation such as cytoplasmic transfer** | |
| Mexico | There are neither statutes nor guidelines. The technology is used. |

## SUMMARY

ICSI as a treatment for male factor infertility has proven to be consistently effective and successful over the years. It is reported to be regularly applied all over the world. Genetic evaluation is recommended in the male partner with impaired spermatogenesis, since there is a high incidence of Y-chromosome deletions in

this group and there exists the risk of directly transmitting this as well as other chromosomal abnormalities to their offspring. Introduction of newer treatment modalities such as IVM, oocyte freezing, and PGD are most often performed with use of ICSI.

Current evidence suggests no increased risk of significant cognitive impairment in ICSI offspring as compared to IVF and naturally born children (9). However, more long-term studies need to be conducted on children born following ART and, specifically, ICSI procedures.

Assisted hatching is being reported to be routinely practiced in most countries. AH does appear to improve pregnancy rates in patients with recurrent IVF failures and in those with frozen thawed embryos. In most countries AH is reported to be most often performed using the simple, standardized, though costly, technique of diode laser hatching.

Cytoplasmic transfer is rarely used, primarily because of safety concerns including the inadvertent introduction of third-party DNA when using heterologous cytoplasm.

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| Table 10.1 Micromanipulation | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| How ART is governed | Country | ICSI allowed under statute | | | Assisted hatching allowed/used | | | | | Other micro-manipulation allowed* | | |
| | | Yes | No | NM | Yes | No | NM | In some units | N/used | Yes | No | NM |
| By statutes | Belgium | + | | | | | unknown | + | | | | + |
| | Bulgaria | + | | | + | | | + | | | | + |
| | Colombia | | | + | + | | | + | | | | + |
| | Croatia | | | unknown | | | unknown | | + | | | unknown |
| | Czech Republic | + | | | + | | | + | | | | + |
| | Denmark | + | | | + | | | + | | | + | |
| | Finland | + | | | + | | | unknown | | | | + |
| | Greece | + | | | + | | | + | | + | | |
| | Hungary | + | | | + | | | + | | | + | |
| | Iceland | | | + | | | + | NM | | | | + |
| | Libya | + | | | + | | | + | | | + | unknown |
| | Portugal | | | + | | | + | NM | | | | + |
| | Slovenia | + | | | + | | | | + | | | + |
| | Tunisia | + | | | | | + | | + | | | + |

| Table 10.1 Micromanipulation (continued) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **How ART is governed** | **Country** | **ICSI allowed** | | | **Assisted hatching allowed/used** | | | | | **Other micro-manipulation** | | |
| | | **Yes** | **No** | **NM** | **Yes** | **No** | **NM** | **In some** | **N/used** | **Yes** | **No** | **NM** |
| **Guidelines** | Australia | + | | | + | | | + | | | + | |
| | Cameroon | + | | | | | + | | + | | | + |
| | Egypt | + | | | + | | | + | | | + | |
| | India | + | | | + | | | + | | + | | |
| | Ireland | + | | | + | | | + | | | | + |
| | Ivory Coast | + | | | | + | | | + | | | unknown |
| | Japan | + | | | | | + | + | | | | + |
| | Philippines | + | | | + | | | + | | | | + |
| | Singapore | + | | | + | | | + | | | + | |
| | Vietnam | + | | | + | | | + | | | | unknown |

| Table 10.1 Micromanipulation (continued) | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| How ART is governed | Country | ICSI allowed | | | Assisted hatching allowed/used | | | | | Other micro-manipulation | | |
| | | Yes | No | NM | Yes | No | NM | In some units | N/used | Yes | No | NM |
| **Both statute and guidelines** | Argentina | + | | | + | | | + | | | | + |
| | Austria | | | + | | | + | + | | | | + |
| | Belarus | | | + | | | + | + | | | | + |
| | Brazil | + | | | + | | | + | | | + | |
| | China | + | | | + | | | + | | | + | |
| | France | + | | | + | | | + | | | + | |
| | Hong Kong | + | | | + | | | + | | | + | |
| | Israel | + | | | + | | | + | | | + | |
| | Italy | + | | | | | + | + | | | | + |
| | Kazakhstan | + | | | + | | | + | | + | | |
| | Korea | | | + | | | + | + | | | | + |
| | Latvia | + | | | | | + | + | | | + | |
| | New Zealand | + | | | + | | | + | | | + | |
| | Norway | + | | | + | | | + | | | + | |
| | Russia | + | | | + | | | + | | | | + |
| | South Africa | + | | | | | + | + | | | + | |
| | Spain | + | | | + | | | + | | | + | |
| | Sweden | + | | | + | | | | + | | + | |
| | Switzerland | + | | | + | | | + | | | + | |
| | Taiwan | + | | | + | | | + | | | | + |
| | Turkey | + | | | | | + | + | | | + | |
| | United Kingdom | + | | | + | | | + | | | + | |
| | United States | + | | | + | | | + | | | + | |

| Table 10.1 Micromanipulation (continued) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| How ART is governed | Country | ICSI allowed | | | Assisted hatching allowed/used | | | | | Other micro-manipulation | | |
| | | Yes | No | NM | Yes | No | NM | In some units | N/used | Yes | No | NM |
| **None** | Chile | | | unknown | | | + | + | | | | + |
| | Democratic Republic of the Congo | + | | | | | + | | + | | + | |
| | Dominican Republic | + | | | | | unknown | + | | | | unknown |
| | Ecuador | | | + | | | + | + | | | | + |
| | Mexico | | | + | | | + | + | | | | + |
| | Panama | | | + | | | + | + | | | | unknown |
| | Peru | + | | | + | | | | + | | | + |
| | Saudi Arabia | + | | | + | | | + | | | + | |
| | Senegal | + | | | | + | | | + | | | + |
| | Togo | | | + | | | + | + | | | | + |
| | Uruguay | + | | | + | | | + | | | + | |
| | Venezuela | + | | | + | | | + | | | + | |
| **Unknown** | Uganda | + | | | | | unknown | unknown | | | | unknown |

N/mentioned: NM; N/used: Not used

*(e.g., cytoplasmic transfer). For cloning see Cloning Chapter

Multiple replies submitted for the country but only one response included in table.

# Chapter 11: Oocyte maturation

## INTRODUCTION

*In vitro* maturation (IVM) consists of culturing immature oocytes *in vitro* to maturity sufficient to permit IVF. IVM requires little or no pharmacologic stimulation, is less expensive than traditional IVF (which requires gonadotropin-induced controlled ovarian superstimulation), and is ideally suited for the management of patients otherwise at risk for hyperstimulation syndrome. Oocyte retrieval, performed on smaller follicles, requires larger bore, specialized needles and elaborate, prolonged culture conditions. ICSI is normally required for fertilization. IVM is ideally suited for younger patients with polycystic ovary disease who are at increased risk of hyperstimulation with traditional gonadotropin therapy. It also is useful for younger oncofertility patients seeking urgent oocyte or embryo cryopreservation when it is difficult to schedule retrieval or gonadotropin therapy should be avoided. IVM retrieval can be performed at any time in the cycle.

## ANALYSIS OF THE SURVEY

***Oocyte maturation:*** Oocyte maturation was reported to be allowed in 29 of the 43 countries with formal statutes, laws, and guidelines, but it is not allowed in 2 (Denmark and Senegal) of the 43 countries. Respondents state that it is restricted by statute in 5 countries and by guidelines in 12. Oocyte maturation was reported to be actively practiced in 20 countries, and oocyte maturation is used in 9 countries as a part of their oocyte cryopreservation practice (Table 11.1).

## DISCUSSION

IVM is an evolving technology and Surveillance 2013 reflects considerably greater use than in 2010. It has not aroused the controversy of other ART therapies, but its efficiency is still in question, as reflected by the comments obtained from respondents in the survey. Although live birth rates have improved, outcomes following long-term storage of gametes or embryos are not clearly established.

## SUMMARY

IVM is a relatively newer technology that is improving and is likely to see increasing use as experience accumulates.

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| Table 11.1 *In vitro* maturation | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Allowed under statute/law/guidelines?** | | | | **Is this determined by?** | | | | | | **Practiced by programs In your country?** | | | | **Comments from respondents** |
| | **A** | **NA** | **NM** | **UNK** | **Guide-lines** | **Law** | **Statute** | **UNK** | **Null** | **None of the above** | **Yes** | **No** | **UNK** | **Null** | |
| Argentina* | | | X | | | | | X | | | X | | | | |
| Australia | X | | | | | | | | | X | X | | | | |
| Austria | X | | | | | | | | | X | X | | | | Only in case of emergency (no mature oocyte collected) |
| Belarus | | | X | | | | | | | X | | X | | | |
| Belgium | X | | | | | | | | | X | X | | | | Only done by a few centers |
| Brazil | | | X | | | | | | | X | X | | | | |
| Bulgaria | X | | | | | | X | | | | X | | | | Only few centers |
| Cameroon | | | X | | | | | X | | | | X | | | |
| Chile | | | X | | | | | | X | | X | | | | |
| China | X | | | | X | | | | | | X | | | | |
| Colombia | | | X | | | | | | | X | | X | | | |
| Croatia | | | X | | | | | X | | | | X | | | |
| Czech Republic | | | X | | | | | | | X | X | | | | IVM is practiced but not used often |

| Table 11.1 *In vitro* maturation (continued) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Allowed under statute/law/guidelines?** | | | | **Is this determined by?** | | | | | | **Practiced by programs In your country?** | | | | **Comments from respondents** |
| | **A** | **NA** | **NM** | **UNK** | **Guide-lines** | **Law** | **Statute** | **UNK** | **Null** | **None of the above** | **Yes** | **No** | **UNK** | **Null** | |
| Democratic Republic of the Congo | | | | X | | | | | | X | | | X | | I have no information about this practice in our unique center |
| Denmark* | | X | | | | X | | | | | X | | | | Under research protocols |
| Dominican Republic | | | | X | | | | X | | | | | X | | |
| Ecuador | | | X | | | | | | | X | | X | | | |
| Egypt | X | | | | | | | X | | | | | X | | |
| Finland | X | | | | | | | | | X | | | X | | Earlier in 2-3 clinics, very seldom nowadays |
| France | X | | | | | | | | | X | X | | | | |
| Greece | | | X | | | | | | | X | X | | | | Since it is not specifically regulated or forbidden, it can be applied |
| Hong Kong* | X | | | | | | | | | X | X | | | | |
| Hungary | | | X | | | | | | | X | X | | | | |
| Iceland | | | X | | | | | | X | | | X | | | |

| Table 11.1 *In vitro* maturation (continued) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Allowed under statute/law/guidelines?** | | | | **Is this determined by?** | | | | | | **Practiced by programs In your country?** | | | | **Comments from respondents** |
| | **A** | **NA** | **NM** | **UNK** | **Guide-lines** | **Law** | **Statute** | **UNK** | **Null** | **None of the above** | **Yes** | **No** | **UNK** | **Null** | |
| India* | X | | | | X | | | | | | X | | | | It is done in polycystic ovary syndrome (PCOS) patients and in patients with history of PCOS |
| Ireland | | | X | | | | | X | | | | X | | | No law |
| Ireland (Republic) | | | X | | | | | | | X | | X | | | |
| Israel | X | | | | X | | | | | | X | | | | Limited |
| Italy | X | | | | | X | | | | | X | | | | |
| Ivory Coast | | | | X | | | | | X | | | | | X | |
| Japan | | | X | | X | | | | | | X | | | | |
| Kazakhstan | X | | | | | | | | | X | | X | | | |
| Latvia* | | | X | | X | | | | | | X | | | | Guidelines are under preparation and accept process |
| Libya* | X | | | | | | X | | | | X | | | | |
| Mexico | | | X | | | | | | X | | X | | | | |
| New Zealand | X | | | | X | | | | | | X | | | | |
| Norway | X | | | | | | X | | | | X | | | | Only a few cycles a year, primarily for one clinic |

| Table 11.1 *In vitro* maturation (continued) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Allowed under statute/law/guidelines?** | | | | **Is this determined by?** | | | | | | **Practiced by programs In your country?** | | | | **Comments from respondents** |
| | **A** | **NA** | **NM** | **UNK** | **Guide-lines** | **Law** | **Statute** | **UNK** | **Null** | **None of the above** | **Yes** | **No** | **UNK** | **Null** | |
| Panama | | | X | | | | | X | | | X | | | | |
| Peru | | | | X | | | | X | | | | X | | | |
| Philippines | | | X | | | | | X | | | X | | | | No law or guidelines regarding the issue |
| Russia* | X | | | | X | | | | | | X | | | | |
| Saudi Arabia | X | | | | | | | | | X | X | | | | |
| Senegal | | X | | | | | | | | X | | X | | | |
| Singapore | X | | | | X | | | | | | | | X | | |
| Slovenia | X | | | | | X | | | | | X | | | | Very rarely |
| South Africa | | | X | | | | | | | X | | | X | | Very rarely now |
| South Korea | | | X | | | | | | | X | X | | | | |
| Spain* | | | | X | | | | X | | | X | | | | In PCO women but very few centers do it |
| Sweden | X | | | | X | | | | | | X | | | | Practiced to a limited extent only, in research |
| Switzerland | X | | | | | | | | | X | X | | | | |
| Taiwan | | | X | | | | | X | | | X | | | | |

| Table 11.1 *In vitro* maturation (continued) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Allowed under statute/law/guidelines?** | | | | **Is this determined by?** | | | | | | **Practiced by programs In your country?** | | | | **Comments from respondents** |
| | **A** | **NA** | **NM** | **UNK** | **Guide-lines** | **Law** | **Statute** | **UNK** | **Null** | **None of the above** | **Yes** | **No** | **UNK** | **Null** | |
| Togo | | | X | | | | | | | X | | X | | | |
| Tunisia | | | X | | | | | | X | | | | | X | |
| Turkey | | | X | | | | | X | | | X | | | | |
| Uganda | | | | X | | | | | X | | | | X | | Not known |
| United Kingdom* | X | | | | X | | | | | | X | | | | In accordance with HFEA Code of Practice |
| Uruguay | X | | | | | | | | | X | | X | | | |
| United States | X | | | | X | | | | | | X | | | | ASRM still considers IVM to be experimental |
| Venezuela | X | | | | | | | X | | | X | | | | In specific cases |
| Vietnam | X | | | | | | | | | X | X | | | | In necessary cases |

**A: Allowed NA: Not allowed NM: Not mentioned UNK: Unknown**

* Multiple replies submitted for the country but only one response included in table.

# Chapter 12: Welfare of the child

## INTRODUCTION

Legislation addressing the welfare of the child has been extensively addressed in a minority of countries, most notably the United Kingdom in their 1990 Human Fertilization and Embryology Act (HFEA), which was discussed in more detail in Surveillance 2010. For example, a formal "Welfare of the Child" assessment is an obligatory part of the fertility clinic evaluation conducted at the first consultation in the United Kingdom. Prospective parents are asked about previous convictions related to harming children, contact with social services regarding care of other children, a history of violence or serious discord within the family, drug or alcohol abuse, the existence of serious mental or physical conditions that might impair their ability to care for a child, and risk to the child of a serious medical condition (1). HFEA requires that these issues be considered before a fertility clinic can consent to provide care. Based upon the previous survey, other countries that do have guidelines or legislation addressing the welfare of the child have considerably less rigorous processes in place.

## ANALYSIS OF THE SURVEY

In the current survey, respondents from 51 countries provided information about the status of guidelines and statutes addressing the welfare of the child (Table 12.1). Ten countries are reported to have enacted laws providing protection, 36 have not, and the status in another 5 countries was unknown by the respondents. Countries with reported statutory protection of the welfare of children include Australia, China, Finland, Hong Kong, Italy, New Zealand, Norway, Slovenia, Sweden, and the United Kingdom. In 2010, respondents from 17 countries provided information about laws that had been enacted to protect the welfare of the child, but 6 of the previous affirmative respondents noted that statutes addressing the welfare of the child did not exist in the current survey. Several of these respondents provided expanded answers and noted that limited resources were in place, such as to provide mechanisms to address birth registries. The response to the same question as it relates to guidelines revealed that 13 countries are reported to have guidelines in place, 34 do not, and the status is unknown by the respondents in an additional 4.

## CONCLUSIONS

In summary, based upon the information reported by the respondents, it does not appear that significant change in the development of laws or guidelines addressing the welfare of the child has occurred over the past three years. The current data set and feedback from respondents are insufficient to determine whether countries have actually rescinded previous legislation addressing the welfare of the child.

## REFERENCES

**1.** www.hfea.gov.uk/1414html

| Table 12.1 Welfare of the child | | |
|---|---|---|
| **Country** | **Laws or guidelines addressing the welfare of the child** | **Comments from respondents** |
| Argentina | Not mentioned | |
| Australia | Yes | Welfare offspring of paramount importance. Individuals considered to be unsuitable parents can be refused treatment. |
| Austria | Not mentioned | |
| Belarus | Not mentioned | |
| Belgium | Not mentioned | Not mentioned in detail, only in general terms |
| Brazil | Not mentioned | |
| Bulgaria | Not mentioned | |
| Cameroon | Not mentioned | |
| Chile | Not mentioned | Not regulated |
| China | Yes | |
| Colombia | Not mentioned | |
| Croatia | Not mentioned | |
| Czech Republic | Not mentioned | |
| Democratic Republic of the Congo | Not mentioned | |
| Denmark | Not mentioned | Welfare of the child is followed in the Danish birth register. |
| Dominican Republic | Unknown | |
| Ecuador | Not mentioned | |
| Egypt | Unknown | |
| Finland | Yes | Some limitations to the performance of ART are based on the consideration of the welfare of the child |
| France | Not mentioned | |
| Greece | Not mentioned | |
| Hungary | Not mentioned | |
| Iceland | | |
| India | Not mentioned | |
| Ireland (Republic) | Not mentioned | |
| Israel | Not mentioned | |
| Italy | Yes | Article 8 of Law 40/2004 equalize them to legitimate offspring conceived naturally. |
| Ivory Coast | Not mentioned | |
| Japan | Unknown | |

| Table 12.1 Welfare of the child (continued) | | |
|---|---|---|
| **Country** | **Laws or guidelines addressing the welfare of the child** | **Comments from respondents** |
| Kazakhstan | Not mentioned | |
| Latvia | Not mentioned | Only about the legal status of the offspring |
| Libya | Not mentioned | |
| Mexico | Not mentioned | |
| New Zealand | Yes | Health and well-being of children 'an important consideration' |
| Norway | Yes | |
| Panama | Not mentioned | |
| Peru | Unknown | |
| Philippines | Not mentioned | |
| Portugal | | |
| Russia | Not mentioned | No |
| Saudi Arabia | Not mentioned | |
| Senegal | Not mentioned | |
| Singapore | Not mentioned | |
| Slovenia | Yes | The best interest of the child should be respected in infertility treatment. |
| South Africa | Not mentioned | No mention in the law |
| South Korea | Not mentioned | |
| Spain | Not mentioned | |
| Sweden | Yes | Parents (to be) should not be too old or sick and of reasonably good psychosocial status to ascertain a reasonably smooth childhood |
| Switzerland | Not mentioned | |
| Taiwan | Not mentioned | |
| Togo | Not mentioned | |
| Tunisia | Not mentioned | |
| Turkey | Not mentioned | |
| Uganda | | No law yet |
| United Kingdom | Yes | In accordance with HFEA Code of Practice, a woman shall not be provided with treatment services unless account has been taken of the welfare of any child who may be born as a result of the treatment (including the need of that child for supportive parenting) and of any other child who may be affected by the birth. |
| Uruguay | Not mentioned | |

| Table 12.1 Welfare of the child (continued) | | |
|---|---|---|
| **Country** | **Laws or guidelines addressing the welfare of the child** | **Comments from respondents** |
| United States | Not mentioned | The law does not mention. The guidelines address it briefly. |
| Venezuela | Not mentioned | N/A |
| Vietnam | Not mentioned | Unknown |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 13: Selective fetal reduction

## INTRODUCTION

Fetal reduction is the technique used to reduce the number of fetuses in a multiple pregnancy to a lesser number. Over the past three decades, there has been an increase in the number of multifetal pregnancies as a result of the increase in the use of ART and other ovulation induction regimens, particularly those involving gonadotropins (1). Between 1980 and 2009, the twin pregnancy rate increased 76%, from 18.9 to 33.3 per 1,000 live births (2). The triplet or greater birth rate increased more than 400% between 1980 and 1998, when it peaked at 1.935 per 1,000 births (3). Between 1998 and 2009, the incidence of high-order multiple deliveries decreased by 29% (3). The reason for this decrease is due to decrease in the number of embryos transferred per cycle as well as increase in the safety and success of fetal reduction procedures. According to the latest published report in 2012, the International Committee Monitoring Assisted Reproductive Technologies (ICMART) Report covering the year 2004 states that worldwide the average number of embryos transferred per cycle was 2.35. Single (16.3%) and double embryo transfers accounted for 73.2% of cycles (4). This chapter deals with the question of selective fetal reduction, its prevalence in practice, the laws surrounding it, and whether it is an option to be considered for higher order multiple pregnancies.

## ANALYSIS OF THE SURVEY

Data provided by respondents from 60 countries were collected (Table 13.1). The countries were evaluated by the respondents on the basis of 4 categories: countries that allow selective fetal reduction by law, those that have guidelines permitting it, those that practice it according to program, and those that practice it only as a custom.

The respondents from countries surveyed provided feedback that 37 countries had a fixed statute regarding selective fetal reduction, out of which 26 countries allowed the practice whereas the remaining 11 did not permit it.

Respondents from 30 countries have mentioned selective fetal reduction in their guidelines, 33 countries practice this by program, and 27 countries practice this as a custom. This last category also includes 3 countries in which the guidelines do not allow selective fetal reduction but it is practiced according to prevailing custom. The number of 3 has shown a significant reduction since the last survey, when 11 countries were reported as practicing selective fetal reduction in spite of statutes or guidelines prohibiting it.

However, of the 26 countries in which selective fetal reduction is allowed by statute or guidelines and where the respondent answered ‘yes’ to the question, ‘Is selective reduction practiced in your country?’ 62% of them are practicing selective fetal reduction, much higher than the 32% shown in the 2010 Surveillance.

Mainly, South American countries are reported to have specific laws prohibiting reduction, which is likely and often prescribed as a consequence of religious beliefs.

## DISCUSSION

The rise in the rate of fetal reduction is due to the increase in the number of IVF and ICSI treatments conducted. In spite of numerous statutes and guidelines governing the number of embryos to be transferred per cycle, there are still many countries reporting that there is transfer of 3 or more embryos, which is likely in the hope of a better success rate. In the 2009 Society for Assisted Reproductive Technologies

(SART) report, less than 2% of all IVF births involve 3 or more babies. The rate of higher order multiple pregnancies increases with increasing serum estradiol concentrations, with younger age of the woman, and with increasing total number of growing follicles (5).

Fetal reduction is now considered by clinicians as a relatively safe procedure, with equivalent pregnancy outcomes. Miscarriage rates were significantly higher when reduction was performed after 15 weeks as compared to early fetal reduction (6). Gonadotropin-IUI carries a significant risk of high-order multiple birth (11.6%) among resulting viable pregnancies (7).

## SUMMARY

This survey of respondents has shown that currently the decision to reduce a pregnancy, especially a twin pregnancy, remains in the hands of the treating physician, to be decided according to the individual patient.

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5. Reduction of twin pregnancy to singleton: does it improve pregnancy outcome? Joseph Hasson et al, The Journal of Maternal-Fetal and Neonatal Medicine, 2011.
6. Risk factors for high-order multiple implantation after ovarian stimulation with gonadotrophins: evidence from a large series of 1878 consecutive pregnancies in a single centre. Rosa Tur et al. Human Reproduction 2001.
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| Table 13.1 Selective reduction | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Allowed by statute** | | | | **Approved by guidelines** | | | | **Practiced in your country** | | |
| | **Allowed** | **Not allowed** | **Not mentioned** | **Unknown** | **Yes** | **No** | **Not mentioned** | **Unknown** | **Yes** | **No** | **Unknown** |
| Argentina | | + | | | | | + | | | + | |
| Australia | | | | | | | | | | | |
| Austria | | | + | | | | + | | + | | |
| Belarus | | | + | | | | + | | + | | |
| Belgium | + | | | | | | | + | + | | |
| Brazil | | + | | | | + | | | + | | |
| Bulgaria | + | | | | + | | | | + | | |
| Cameroon | | | + | | | | + | | + | | |
| Chile | | + | | | | + | | | | + | |
| China | + | | | | + | | | | + | | |
| Colombia | | | + | | | | + | | | | + |
| Croatia | | | + | | | | | + | | + | |
| Czech Republic | + | | | | + | | | | + | | |
| Democratic Republic of the Congo | | | + | | | + | | | | + | |
| Denmark | + | | | | + | | | | + | | |
| Dominican Republic | | + | | | | | | + | | + | |
| Ecuador | | | + | | | + | | | | + | |
| Egypt | + | | | | + | | | | + | | |
| Finland | + | | | | | | + | | | | + |
| France | + | | | | + | | | | + | | |
| Greece | + | | | | | | + | | + | | |
| Hong Kong | + | | | | + | | | | + | | |
| Hungary | + | | | | | | + | | + | | |
| Iceland | | | + | | | | | | | | |
| India | + | | | | + | | | | + | | |
| Ireland | | + | | | | + | | | | + | |
| Israel | + | | | | + | | | | + | | |
| Italy | | | + | | | | + | | + | | |
| Ivory Coast | | | | + | | | + | | | + | |
| Japan | | | | + | | | + | | | | + |
| Kazakhstan | + | | | | | + | | | | + | |

| Table 13.1 Selective reduction (continued) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Country | Allowed by statute | | | | Approved by guidelines | | | | Practiced in your country | | |
| | Allowed | Not allowed | Not mentioned | Unknown | Yes | No | Not mentioned | Unknown | Yes | No | Unknown |
| Latvia | | + | | | | + | | | + | | |
| Libya | + | | | | | | + | | + | | |
| Mexico | | + | | | | | | | | | + |
| New Zealand | + | | | | + | | | | + | | |
| Norway | | | + | | | | + | | | + | |
| Panama | | | + | | | | + | | | + | |
| Peru | | | | + | | + | | | | + | |
| Philippines | | + | | | | + | | | | + | |
| Portugal | | | | | | | | | | | |
| Russia | + | | | | + | | | | + | | |
| Saudi Arabia | | | | + | | | | + | | | |
| Senegal | | + | | | | | + | | | + | |
| Singapore | | + | | | | + | | | | + | |
| Slovenia | + | | | | + | | | | | + | |
| South Africa | + | | | | | | + | | + | | |
| South Korea | | | + | | | | + | | + | | |
| Spain | | | + | | | | + | | + | | |
| Sweden | + | | | | | | | | + | | |
| Switzerland | + | | | | | | + | | + | | |
| Taiwan | + | | | | | + | | | + | | |
| Togo | | | + | | | | + | | | + | |
| Tunisia | + | | | | + | | | | + | | |
| Turkey | | + | | | | + | | | | + | |
| Uganda | | | | + | | | | + | | + | |
| United Kingdom | + | | | | + | | | | + | | |
| Uruguay | | | + | | | | + | | + | | |
| United States | + | | | | + | | | | + | | |
| Venezuela | | + | | | | + | | | | + | |
| Vietnam | + | | | | + | | | | + | | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 14: Preimplantation genetic diagnosis

## INTRODUCTION

There has been in excess of 10,000 births worldwide from over 50,000 IVF-PGD cycles since the case first reports in 1990 (1,2). PGD most commonly involves removal of 1 or 2 blastomeres at the 8-cell stage on day 3 of *in vitro* development. This is followed by genetic analysis using fluorescent in situ hybridization (FISH) analysis of 5-12 chromosomes, polymerase chain reaction (PCR) whole genome amplification (WGA), microarrays, or next generation sequencing technology (NGS) (2-10). Unaffected embryos are transferred back on day 4 or 5. Since embryos with genetic abnormalities are discarded, PGD requires couples to make a moral distinction between termination of an implanted pregnancy and the discarding of affected, non-transferred embryos (1).

There are 9 general categories for which PGD is currently in use:

*1. Autosomal single gene disorders (5-7)*
*2. Chromosomal rearrangements (5-7)*
*3. X-linked diseases (5-7)*
*4. Human leukocyte antigen (HLA) typing (5-7)*
*5. Cancer predisposition genes (8)*
*6. Mitochondrial DNA disorders (9)*
*7. Preimplantation genetic screening (PGS) for embryonic aneuploidy (5-7)*
*8. Adult onset disorders (10)*
*9. Non-medical sex selection (5,6)*

## ANALYSIS OF THE SURVEY

The first category surveyed what PGD is practiced under (Table 14.1). PGD is reported to be allowed in 38 of the 46 countries with statutes, laws, and guidelines. It is not reported as being mentioned in the statutes of 5 of these 44 countries, and it is not allowed in 2 of the 46: the Philippines and Switzerland. PGD is reported as being used in 44 of the 46 countries. In 8 of these countries, respondents state that PGD is restricted to specific hereditary disorders: Denmark, Sweden, Latvia, Libya, Senegal, Venezuela, Slovenia, and Korea (Table 14.1).

Preimplantation genetic screening (PGS) was specifically surveyed (Table 14.1). It is reported to be allowed in 26 of the 46 countries with statutes, laws, and guidelines. It is reported as not being mentioned in the statutes, laws, and guidelines of 10 of these 46 countries. Respondents replied that it is not allowed in 7 of the 46 countries: Kazakhstan, Norway, Sweden, Libya, Philippines, Singapore, and Slovenia. PGS is reported as being used in 32 of these 46 countries; however, its utilization over the past 5 years has been reported as showing a decline (with evidence indicating lack of effectiveness for increasing birth rates). This negative trend in PGS utilization may be reversing in the wake of technology advances introduced in the past year.

Finally, PGD practice in 5-12 countries with neither statutes nor guidelines was reported upon by respondents who were surveyed (Table 14.1). In these countries, PGD is reported as not being practiced in 3: Togo, Democratic Republic of the Congo, and Senegal (Table 14.1).

## DISCUSSION

This survey, when compared to Surveys 2010, 2007, and 2004, shows PGD as an increasing percentage of assisted reproductive clinical service effort throughout the world. Its application, however, is often reported as being restricted by statute or local clinical tradition. It is reported as not being allowed in only 2 countries. However, it is reported as being used in 44 of the 46 countries whose respondents provided feedback on this issue and where it is practiced with statutes or guidelines. In the 5 countries with no guidelines, it was reported as not being practiced in 3 of the 12. Now a well-established and reliable procedure, PGD has a low error rate when performed in skilled hands. Drawbacks remain the high cost and inefficiency of IVF as a platform, limitations in culture to blastocyst, and compromised birth rates even in fertile women because PGD selects embryos for transfer.

This report provides no information on how PGD is performed, how often it is performed, who performs it, or on efficacy. There are regional organizations focusing on these issues by collecting data and comparing cumulative data in an attempt to answer some of these questions. One such group is the ESHRE PGD Consortium. Its most recent report, published in 2012, is entitled: *ESHRE PGD Consortium: 10 Years of Data Collection* (12). This report covers data from 57 Centers. It includes a follow-up of the babies born in those centers (12).

In the United States, PGD is considered experimental for purposes of reimbursement and is usually not covered by insurance except for single gene disorders and selected chromosomal defects (Table 14.3). Demand for PGD in the United States, European Union, and Middle East, however, is expected to expand into substantially larger markets of not-infertile couples who, because they are carriers, are at risk for transmission of genetic disorders to their progeny and are reluctant to have children. In the near future, identifying risks for some common but devastating genetic diseases will be possible by PGD. The availability of new molecular genetic tests, public initiatives surrounding specific genetic diseases, and increasing internet marketing of tests and identification of carriers are expected to increased demand for PGD worldwide (2-5,7).

## SUMMARY

PGD in Surveillance 2013, compared to past surveys, is reported as being increasingly available worldwide. It provides easily proven benefits, is generally considered safe, and has a low frequency of errors. Because embryonic aneuploidy is a common cause of IVF failure, PGS for embryonic aneuploidy has been the most frequent, albeit controversial, indication for its use reported in many countries. PGS may, in some cases, increase IVF birth rates. PGD clearly prevents women from delivering offspring with serious genetic disorders, avoids terminations, and brings peace of mind to many couples that otherwise are fearful or simply would not have children.

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| Table 14.1 PGD | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| How ART is governed | COUNTRY | PGD | | | | PGD for embryo screening (aneuploidy) | | | |
| | | Allowed | Not allowed | Used | Not used | Allowed | Not allowed | Used | Not used |
| Statutes/law | Belgium | + | | + | | + | | | |
| | Bulgaria | + | | + | | + | | + | |
| | Colombia | | | + | | | | + | |
| | Croatia | | | | + | | | | + |
| | Czech Republic | + | | + | | + | | + | |
| | Denmark | + | | + | | | + | | + |
| | Finland | + | | + | | + | | | |
| | Greece | + | | + | | + | | + | |
| | Hungary | | | + | | | | + | |
| | Iceland | | | | | | | | |
| | Ireland | | | | + | | | | + |
| | Libya | + | | + | | + | | + | |
| | Portugal | | | | | | | | |
| | Slovenia | + | | + | | | + | | + |
| | Tunisia | + | | | + | | | | + |
| | United Kingdom | + | | + | | + | | + | |
| | | | | | | | | | |
| Guidelines | Argentina | + | | + | | | | + | |
| | Cameroon | + | | | + | | | | + |
| | Egypt | + | | + | | + | | | + |
| | India | + | | + | | + | | + | |
| | Ivory Coast | + | | | + | + | | | + |
| | Japan | + | | + | | | + | | + |
| | Philippines | | + | | + | | + | | + |
| | Singapore | + | | + | | | + | | + |
| | Vietnam | + | | + | | + | | + | |

| Table 14.1 PGD (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| How ART is governed | Country | PGD | | | | PGD for embryo screening (aneuploidy) | | | |
| | | Allowed | Not allowed | Used | Not used | Allowed | Not allowed | Used | Not used |
| Both statutes/law and guidelines | Australia | + | | + | | + | | + | |
| | Austria | | | + | | | | | + |
| | Belarus | | | | | | | | |
| | Brazil | + | | + | | + | | + | |
| | China | + | | + | | + | | + | |
| | France | + | | + | | | + | | + |
| | Hong Kong | + | | + | | | | + | |
| | Israel | + | | + | | + | | + | |
| | Italy | + | | + | | + | | + | |
| | Kazakhstan | + | | + | | + | | + | |
| | Latvia | | | + | | | | + | |
| | New Zealand | + | | + | | + | | + | |
| | Norway | + | | + | | | + | | + |
| | Russia | + | | + | | + | | + | |
| | South Africa | + | | + | | + | | + | |
| | Korea | | | + | | | | + | |
| | Spain | + | | + | | | | + | |
| | Sweden | + | | + | | | + | | + |
| | Switzerland | | + | | + | + | | | + |
| | Taiwan | + | | + | | + | | + | |
| | Turkey | + | | + | | + | | + | |
| | United States | + | | + | | + | | + | |

| Table 14.1 PGD (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **How ART is governed** | **COUNTRY** | **PGD** | | | | **PGD for embryo screening (aneuploidy)** | | | |
| | | **Allowed** | **Not allowed** | **Used** | **Not used** | **Allowed** | **Not allowed** | **Used** | **Not used** |
| **Neither statutes/law nor guidelines** | Chile | | | + | | | | + | |
| | Democratic Republic of the Congo | | | | + | | | | + |
| | Dominican Republic | | + | | | | + | | |
| | Ecuador | | | | | | | | |
| | Mexico | + | | + | | | | + | |
| | Panama | | | | | | | | |
| | Peru | + | | + | | + | | + | |
| | Saudi Arabia | + | | + | | + | | + | |
| | Senegal | | | | + | | | | + |
| | Togo | | | | + | | | | + |
| | Uruguay | + | | + | | + | | + | |
| | Venezuela | + | | + | | + | | + | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 15: IVF surrogacy

## INTRODUCTION

There has been persistent confusion about terminology and the definitions of the different forms of IVF practices that involve surrogacy. It is common practice to use the terms "surrogate host," "surrogate mother," or "surrogate" for the woman who carries and delivers a baby for another couple. The terms "IVF surrogacy," "gestational surrogacy," and "full surrogacy" all are used to refer to treatments in which the gametes of the "genetic couple," "commissioning couple," or "intended parents" in a surrogacy arrangement are used to produce embryos, which subsequently are transferred to a woman who agrees to act as a host for these embryos. The "surrogate host" is therefore genetically unrelated to any offspring that may be born as a result of this arrangement. This IFFS survey addresses only this latter form of surrogacy. It does not cover "natural surrogacy" or "partial surrogacy," in which the intended host is inseminated with the semen of the husband of the "commissioning couple"; any resulting child from this arrangement is, therefore, genetically related to the host. This type of surrogacy does not require the assistance of fertility clinics or IVF technology.

IVF surrogacy is complex with potential conflicts of interest and it is essential that the legal circumstances governing surrogacy in each country be fully understood. Careful medical assessment of both parties prior to entering into an IVF surrogacy arrangement is essential, and full counseling should be offered to all parties. Full and informed legal advice from an adviser experienced in the laws of the country in which the treatment is to be carried out, and, if different, in the country of domicile of the couple, is mandatory. The terms used in this survey for the couple who initiate the surrogacy arrangement and whose gametes are used will be known as the "genetic couple" and the woman who subsequently carries the child will be known as the "surrogate host."

### *Indications for "gestational surrogacy"*

The principal indications for treatment by "IVF surrogacy" are:

1. Women without a uterus but with one or both ovaries functioning:
    a. Women with congenital absence of the uterus
    b. Women who have had a hysterectomy for carcinoma or other reasons
2. Women who have suffered recurrent miscarriages and for whom the prospect of carrying a baby to term is remote. Related to this group, women who have repeatedly failed to achieve a pregnancy following IVF treatment are also considered.
3. Women with certain medical conditions that may make pregnancy life-threatening but for whom the long-term prospects for health are good.

   Requests for career or social reasons are not considered to be appropriate indications.

## ANALYSIS OF THE SURVEY

The questions asked in this 2013 survey were:

- Is IVF surrogacy (i.e., the use of gametes of both prospective parents where the female partner does not have a functioning uterus) allowed under the guidelines?
- Are there special stipulations, and if so, what are they?
- Is IVF surrogacy used by some programs in your country?

This analysis is limited by the number of replies to the worldwide questionnaire that was sent out. In the 2010 survey, of a total of respondents from 105 countries polled, only 71 (68%) responded to the questions about surrogacy, whereas in this 2013 survey, replies were received from respondents from 62 countries. Of those respondents who did not respond to the survey questions, it is known that most countries do not condone IVF surrogacy - mainly respondents cite for religious reasons. From Table 15.1 below, it can be seen that of the respondents from 62 countries, 19 (31%) allow IVF surrogacy by statute or guidelines, 24 (39%) do not allow it, and 14 countries (23%) do not mention IVF surrogacy at all in any guidelines or law. In 23 of the 62 countries (37%), IVF surrogacy was reported to be practiced, but respondents from at least 9 of these countries claim to have no statutes or guidelines.

Quite specific stipulations about IVF surrogacy have been reported by the survey respondents for their respective countries:

- In Australia, the birth mother must be on the birth certificate; however, different states have different regulations. Only "altruistic" surrogacy (not for profit) is allowed.
- Belgium is regulated by a separate law on IVF surrogacy.
- In Brazil, the surrogate host must be related to the commissioning husband or wife, but exemptions may be allowed by regional medical councils. No payment is allowed.
- In Bulgaria, a bill is pending before their parliament.
- In the Czech Republic, surrogacy is performed. Although it is not allowed, it is not expressly forbidden.
- In Greece, there must be a valid medical indication, court approval is required, and no payment is allowed.
- Hong Kong only allows "full" or IVF surrogacy and couples must be married.
- The parliament of Israel has passed a special law on surrogacy, which permits surrogacy.
- Most countries in which the Islamic faith is predominant do not allow surrogacy.
- In New Zealand, each IVF surrogacy case must be submitted to The National Ethics Committee on ART (ECART).
- Russia requires that any surrogate host be 20-35 years of age and have already had at least one child of her own.
- South Africa requires that IVF surrogacy only be offered to residents, and court approval is required. IVF surrogacy only is allowed and the host must have had at least one child herself.
- In Thailand, the birth mother is the legal mother and the genetic couple must adopt any child produced by surrogacy.
- In the United Kingdom, there must be a medical indication and no payment to the host, other than for "expenses," is allowed.
- In the United States, there are generally no limitations, but some states do not allow payment.

## DISCUSSION

Treatment by IVF surrogacy remains a controversial issue worldwide. Of the respondents from 62 countries, only 19 (31%) state that IVF surrogacy is allowed and actually performed, and in an additional 9 countries, IVF is reported to be practiced in the absence of any guidelines or law. Of those countries in which IVF surrogacy is reported to be performed and have available statistics, IVF surrogacy only accounts

for approximately 0.05%-0.2% of IVF treatment cycles. However, there are a number of countries in which surrogacy reported to be increasingly offered to couples traveling from other countries – popularly known as "reproductive tourism" or "cross border reproductive care" – because it is either banned in their own countries, or because the treatment is much less expensive. This trend appears to be raising concern and, for example, recently has resulted in some commissioning couples being unable to adopt or gain citizenship for their children upon return to their own countries. Even in cases in which legal contracts were drawn up between the parties involved, problems have arisen, particularly when the treatment is conducted in a country other than the country of residence.

Payment of surrogate hosts is reported as continuing to be an issue that provokes much debate. Respondents from many countries cite that there are bans on payment to surrogate hosts, which effectively and practically has resulted in not enough women willing to become surrogates. In these countries, it is reported that surrogate hosts tend more often to be related to or be personal friends of the commissioning couple and who are willing to go through treatment, pregnancy, and labor for their family member or friend, and they are only allowed to receive "reasonable expenses." Other countries are reported to allow payment of surrogate hosts, which appears to make available more surrogate hosts for couples who are searching. This issue has been raised and is of particular concern in some less-developed countries in that it may be promoting the commercialization of surrogacy and encourage "reproductive tourism" – or "cross border care" – which may sacrifice safety. India, in particular, is reported to be experiencing a major increase in treatments involving IVF surrogacy. In India, it is reported that a payment of the surrogate hosts is allowed and the costs may be more nominal when compared with other countries where surrogate hosts are paid.

Recent, relatively small studies have provided reassurance regarding the psychological or physical health of the children born as a result of IVF surrogacy treatment and for the well-being of the surrogate hosts and the commissioning couples (1,2).

In most countries, the "birth mother" has always been the legal mother of a child. IVF surrogacy, in which any child born is not genetically related to the birth mother, has complicated this general rule, and many countries or their states have reported to have changed the rules to allow the "genetic parents" to be the legal parents at the birth of the child. These issues, as well as others - for example when the host has changed her mind and wished to keep the child, and when couples separate - have made IVF surrogacy considerably more challenging and new, unanticipated circumstances are arising that are not or may not be sufficiently addressed by laws or guidelines. However, the majority of cases, if managed with the utmost care with regard to the compatibility of the couples and with appropriate counseling and legal advice, proceed without problems and provide a positive and successful treatment option for a small group of women who otherwise would be unable to have their own genetic children.

Both fertility societies, ESHRE and ASRM, have considered the difficult issue of IVF surrogacy and the ethical issues surrounding practices related to it (3,4,5) and have issued guidelines for their members for the small group of women who require this very specialized treatment.

## SUMMARY

IVF surrogacy is a useful treatment option for women who have no uterus or are unable to bear children for other medical reasons. It allows the commissioning or genetic couple to have their own genetic children. It must be conducted with great attention to counseling and legal issues. However, respondents have reported that IVF surrogacy still is not allowed in the majority of their countries. Where respondents have provided

feedback that it is allowed, there are concerns about the commercialization of surrogacy, potential for the exploitation of surrogate hosts, and an increase in inter-country "reproductive tourism" or "cross border reproductive care."

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| Table 15.1 Surrogacy | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is IVF surrogacy allowed under the guidelines?** | | | | | **Is IVF surrogacy used?** | | | |
| | **A** | **NA** | **NM** | **UNK** | **Comments from respondents** | **YES** | **NO** | **UNK** | **Comments from respondents** |
| Argentina* | | | + | | | | + | | |
| Australia | + | | | | Altruistic surrogate, not for profit, must agree to legal proceedings/guidelines | + | | | |
| Austria | | | + | | | | + | | |
| Belarus | + | | | | | | | | |
| Belgium | | | + | | | + | | | |
| Brazil | + | | | | The surrogate must be family, or special situations are studied on regional Medical Councils. | + | | | |
| Bulgaria | | + | | | There is a bill that is not voted yet by the Parliament. | | + | | |
| Cameroon | + | | | | Surrogacy can be authorized in some situations when uterus absent. | + | | | It can be possible. |
| Chile | | | | | | | | + | |
| China | | + | | | | | + | | |
| Colombia | | | + | | | + | | | Some centers carry it out, but the couples tend to travel to the United States where it is allowed to give birth under these circumstances. |
| Croatia | | | | + | | | + | | |
| Czech Republic | | | + | | It isn't allowed but also not forbidden, that's why surrogacy is performed. | + | | | |
| Democratic Republic of the Congo | | | + | | | | + | | |
| Denmark* | | + | | | No | | + | | |
| Dominican Republic | | | | + | | + | | | |
| Egypt | | + | | | Unknown | | + | | |
| Finland | | + | | | No | | + | | Prohibited by law |
| France | | + | | | No special stipulation, just not allowed | | + | | |

| Table 15.1 Surrogacy (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is IVF surrogacy allowed under the guidelines?** | | | | | **Is IVF surrogacy used?** | | | |
| | **A** | **NA** | **NM** | **UNK** | **Comments from respondents** | **YES** | **NO** | **UNK** | **Comments from respondents** |
| Greece | + | | | | Surrogacy is allowed after a Court Decision before the procedure under the following conditions: 1. Medical reason for not being able to carry the pregnancy, 2. Written consent of all parties involved, 3. No payment but compensation of expenses | + | | | |
| Hong Kong* | + | | | | The couple intending to undergo treatment must be married; gametes used must be from the same couple. | + | | | |
| Hungary | | + | | | Strictly prohibited, no stipulations | | + | | Not allowed |
| India* | + | | | | No woman < 21 and > 45 years of age shall be eligible to act as surrogate as per the guidelines. Not more than 3 embryos are transferred in the surrogate's uterus. Surrogacy is offered if female partner is having Müllerian agenesis, congenital uterine anomalies, severe intrauterine adhesion refractory to lysis of adhesions, post-hysterectomy patient, provided no woman shall act as a surrogate for more than 3 successful births in her life time | + | | | |
| Ireland* | | | + | | | | + | | |
| Israel | + | | | | Special law | + | | | |
| Italy | | + | | | | | + | | Surrogacy is prohibited |
| Ivory Coast | | | | + | | | | + | |
| Japan | | + | | | Surrogacy is prohibited by the guideline from Japan Society of Obstetrics and Gynecology (JSOG). | | + | | |
| Kazakhstan | + | | | | | + | | | |
| Latvia* | | | + | | | + | | | |

| Table 15.1 Surrogacy (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is IVF surrogacy allowed under the guidelines?** | | | | | **Is IVF surrogacy used?** | | | |
| | **A** | **NA** | **NM** | **UNK** | **Comments from respondents** | **YES** | **NO** | **UNK** | **Comments from respondents** |
| Libya* | | + | | | Prohibited | | + | | Not allowed |
| Mexico | | | + | | | + | | | |
| New Zealand | + | | | | Case by case approval by ethics committee | + | | | Case by case approval by ethics committee |
| Norway | | + | | | | | + | | |
| Panama | | | + | | | | | | |
| Peru | + | | | | | + | | | |
| Philippines | | + | | | Ethical guidelines, IVF only within married couples, no third-party at least | | + | | |
| Russian Federation* | + | | | | The surrogate mother must have at least one own healthy child. The age of surrogate mother is from 20 until 35. | + | | | |
| Saudi Arabia | | + | | | Not applicable | | + | | |
| Senegal | | + | | | | | + | | |
| Singapore | | + | | | | | + | | |
| Slovenia | | + | | | Prohibited | | + | | Prohibited |
| South Africa | + | | | | Stipulated in the Children's Act. A high court order by a judge is necessary for each patient before starting the procedure. | + | | | A high court order is necessary and this is only allowed for South African commissioning parents |
| South Korea | | | + | | | + | | | |
| Spain* | | + | | | No stipulations because it is not allowed | | + | | |
| Sweden | | + | | | Regulated by law | | + | | |
| Switzerland | | + | | | Not allowed | | + | | |
| Taiwan | | + | | | | | + | | |
| Togo | | | + | | | | + | | |
| Tunisia | | + | | | | | + | | |
| Turkey | | + | | | | | + | | |
| Uganda | + | | | | | + | | | |
| United Kingdom* | + | | | | Surrogacy Arrangement Act | + | | | |
| Uruguay | | + | | | | | + | | |

| Table 15.1 Surrogacy (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is IVF surrogacy allowed under the guidelines?** | | | | | **Is IVF surrogacy used?** | | | |
| | **A** | **NA** | **NM** | **UNK** | **Comments from respondents** | **YES** | **NO** | **UNK** | **Comments from respondents** |
| United States | + | | | | No restrictions in most states, although in some it is not legal to pay the gestational carrier (surrogate) | + | | | Commonly, but not by all programs. Agencies generally find the surrogates. |
| Venezuela | + | | | | In specific cases | + | | | In specific cases |
| Vietnam | | + | | | No comment | | + | | |

**A: Allowed NA: Not allowed NM: Not mentioned UNK: Unknown**

* Multiple replies submitted for the country but only one response included in table.

# Chapter 16: Experimentation on the embryo

## INTRODUCTION

Experimentation on the embryo encompasses a spectrum of investigative activities ranging from subtle changes in media intended to improve culture results to alterations of the genome with a myriad of potential salutary and harmful effects. Experimentation involving embryos intrinsically creates an ethical conflict between the desire to prevent and alleviate human suffering and the obligation to respect the value of human life, concomitant with the global variability of an accepted understanding of when life begins. (See Status of the conceptus, Chapter 18). There has been an extensive literature reviewing these conflicts, controversies, and acceptable parameters in which to conduct embryo research (1,2). These controversies represent the core of the debate about the ethical legitimacy of stem cell research. Recent progress in that field has made the potential benefits more compelling but has not allayed the concerns of those parties emphasizing inherent harm to the embryo. There is extraordinary variety in the approaches that the various countries that permit experimentation have undertaken to address these issues. These policies have become the most significant determinant of whether or not stem cell research is conducted in the affected country. A few notable changes have been reported to occur since the 2010 survey.

Argentina recently adopted new ethical guidelines that the respondents state now permit embryo experimentation on non-viable embryos with stringent experimental protocols required, but otherwise there appears to be little change in national positions regarding embryo experimentation over the past 3 years (3). Respondents from a clear majority of nations still report the prohibition of embryo experimentation. Respondents from only one country, China, stated that reproductive cloning was allowed with restrictions.

## ANALYSIS OF THE SURVEY

In the 2013 edition of Surveillance, respondents were specifically asked about national practices regarding regulation of reproductive and therapeutic cloning, research on embryonic stem cells, potential to donate embryos for stem cell research, opportunities to perform research on fetal and adult stem cells, and control of gene therapy research. Overall, respondents from 54 countries addressed the survey questions regarding the status of embryo experimentation. Twenty-two replied affirmatively to the question, "In your country, is the use of human pre-embryos for experimental purposes an acceptable procedure by statute, guideline, cultural consensus or recognized prevailing religious decree," 29 answered no, and 3 checked "unknown" (Table 16.1). Specific responses to each question and related comments from the respondents are listed in Table 16.2. When embryo experimentation is allowed, third-party approval has been reported to be a near universal requirement. Most of these countries have established a maximum age for the embryo, typically 14 days, beyond which experimentation is prohibited. This topic is further addressed in Chapter 18.

## SUMMARY

Experimentation on the embryo remains a contentious issue and for the respondents from the majority of countries represented in this survey, experimentation is not allowed. Although significant progress in stem cell research has been reported in the literature over the past 3 years, only 1 country, Argentina, has been reported to have modified its previous policy to permit experimentation on embryos under limited conditions.

## REFERENCES

1. National Institutes of Health, Report of the Human Embryo Research Panel: Final Draft. September 27, 1994. Bethesda, MD: National Institutes of Health, 1994

2. http://www.chrt.org.hk/english/embryo/embryo.html
3. http://www.samer.org.ar/docs/codigo_de_etica_de_reproduccion.pdf

| Table 16.1 Experimentation on the preimplantation embryos | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is this an acceptable procedure?** | | | | **What dictates this?** | | | | | |
| | **Yes** | **No** | **Unknown** | **Comments from the respondents** | **Guidelines** | **Law** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| Argentina* | X | | | | X | | | | | Recent publication of SAMeR's ethical guidelines, limited to non-viable embryos, under strict experimental protocols |
| Australia | | | | | | | | | | |
| Austria | | X | | | | X | | | | |
| Belarus | | | | | | | | | | |
| Belgium | X | | | | | X | | | | Approval needed by local Institutional Review Board (IRB) and by Federal Commission for Embryo Research. Dual approval is needed. |
| Brazil | X | | | Frozen embryos that will not be transferred, 3 years after freezing with couple's consent | | X | | | | A Federal Ethic Committee |
| Bulgaria | X | | | The patients should declare that they donated their embryos for research purpose. | | X | | | | |
| Cameroon | | X | | | X | | | | | |
| Chile | | X | | | | | | | | |
| China | | X | | | | X | | | | |
| Colombia | | X | | The criminal law and the General Attorney | | | | X | | |
| Croatia | | X | | | | X | | | | |

| Table 16.1 Experimentation on the preimplantation embryos (continued) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is this an acceptable procedure?** | | | | **What dictates this?** | | | | | |
| | **Yes** | **No** | **Unknown** | **Comments from the respondents** | **Guidelines** | **Law** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| Czech Republic | X | | | | | X | | | | The law on research on human embryonic stem cells and related activities and amending certain related acts |
| Democratic Republic of the Congo | | X | | | | | X | | | |
| Denmark* | X | | | Only for research and given by the ethical committees | | X | | | | |
| Dominican Republic | | X | | | | | | | | |
| Ecuador | | | | | | | | | | |
| Egypt | X | | | | X | | | | | |
| Finland | X | | | | | X | | | | |
| France | X | | | 14 days limit | | X | | | | Only under approved research programs |
| Greece | X | | | Differentiation between research leading to pregnancy and not leading to pregnancy. In both cases up to 14 days conceptuses | | X | | | | Specific approval is mandatory in both situations by the ART Authority. |
| Hong Kong* | X | | | | X | | | | | The Council on Human Reproductive Technology in Hong Kong http://www.chrt.org.hk/ |

| Table 16.1 Experimentation on the preimplantation embryos (continued) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is this an acceptable procedure?** | | | | **What dictates this?** | | | | | |
| | **Yes** | **No** | **Unknown** | **Comments from the respondents** | **Guidelines** | **Law** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| Hungary | X | | | | | X | | | | Scientific Ethics Committee of Ministry of Health |
| Iceland | | | | | | | | | | |
| India* | X | | | Up to 14-day embryos can be used for experimenta-tion. | X | | | | | Indian Council of Medical Research |
| Ireland | | X | | Irish Medical Council Guidelines prohibit experimenta-tion on human embryos. | X | | | | | |
| Ireland (Republic) | | X | | | | | | X | | |
| Israel | | | X | | | | | | | |
| Italy | | X | | | | X | | | | |
| Ivory Coast | | X | | | | | | | | |

| Table 16.1 Experimentation on the preimplantation embryos (continued) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is this an acceptable procedure?** | | | | **What dictates this?** | | | | | |
| | **Yes** | **No** | **Unknown** | **Comments from the respondents** | **Guidelines** | **Law** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| Japan | X | | | Guidelines from Ministry of Education, Culture, Sports, Scientific and Technology (MEXT) Guidelines from Ministry of Health, Welfare and Labour (MHWL) Guidelines from Japan Society of Obstetrics and Gynecology (JSOG) | X | | | | | Application is necessary to MEXT or MHWL or JSOG and depends on the research topics |
| Kazakhstan | | X | | Not required | | X | | | | |
| Latvia* | | X | | Look above the copy of law. | | X | | | | |
| Libya* | | X | | | | | | | | |
| Mexico | X | | | | | | | | X | |

| Table 16.1 Experimentation on the preimplantation embryos (continued) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is this an acceptable procedure?** | | | | **What dictates this?** | | | | | |
| | **Yes** | **No** | **Unknown** | **Comments from the respondents** | **Guidelines** | **Law** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| New Zealand | | X | | Embryo experimenta-tion is not an 'Established procedure,' therefore would need approval by the Minister of Health. The Minister has not given approval. | X | | | | | |
| Norway | X | | | | | | | | | |
| Panama | | | | | | | | | | |
| Peru | | X | | | | | | X | | |
| Philippines | | X | | Philippine Society of Reproductive Endocrinology and Infertility (PSREI) 2011 ethical guidelines on ART | X | | | | | |
| Portugal | | | | | | | | | | |
| Russia* | | X | | | | | | | X | |
| Saudi Arabia | | | X | | | | | | | |
| Senegal | | X | | | | | | | X | |
| Singapore | | X | | | X | | | | | |

| Table 16.1 Experimentation on the preimplantation embryos (continued) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is this an acceptable procedure?** | | | | **What dictates this?** | | | | | |
| | **Yes** | **No** | **Unknown** | **Comments from the respondents** | **Guidelines** | **Law** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| Slovenia | X | | | Only on surplus embryos, good medical interest | | X | | | | Should be approved by Ethics Committee and by Committee for Assisted Reproduction of Slovenia |
| South Africa | X | | | Need permission of the Minister of Health and permission of the patients | | X | | | | National Department of Health |
| South Korea | X | | | Bioethics and Safety Act | | X | | | | Ministry of Health, Welfare and Family Affairs Institutional Review Board |
| Spain* | X | | | | | X | | | | |
| Sweden | X | | | Within 2 weeks, may not be transferred to the uterus afterwards | | X | | | | |
| Switzerland | | X | | | | X | | | | |
| Taiwan | | X | | | | | | | | |
| | | | | | | | | | | |
| Togo | | | X | | | | | | | |
| Tunisia | | X | | | | X | | | | |
| Turkey | | X | | | | | | | X | |
| Uganda | | X | | We do not have guidelines yet, so most of these questions do not apply | | | | | | |

| Table 16.1 Experimentation on the preimplantation embryos (continued) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Country** | **Is this an acceptable procedure?** | | | | **What dictates this?** | | | | | |
| | **Yes** | **No** | **Unknown** | **Comments from the respondents** | **Guidelines** | **Law** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| United Kingdom* | X | | | There must be ethical approval and HFEA approval for some research projects | | X | | | | Medical Research Council - but there are several funding bodies |
| Uruguay | | X | | | | | | | | |
| United States | | X | | Federal law states there are no funds for research on human embryos. Embryos can be donated to specific programs that have funding (e.g., the California Institute for Regenerative Medicine [CIRM]). | | X | | | | CIRM has specific requirements, as does the University of California at San Francisco and Stanford, both of which will accept embryos for research performed under their research protocols but not using any federal funds. They would use state of California funds from CIRM or private funding. |
| Venezuela | | X | | | | | | | X | |
| Vietnam | | X | | | X | | | | | |

* Multiple replies submitted for the country but only one response included in table.

## Table 16.2 Research

### Is the following research possible in your country?

| Country | Reproductive cloning | | | Therapeutic cloning | | | | Research on embryonic stem cells | | | | Donate unused embryos for stem cell research | | | | Research on fetal stem cells | | | | Research on adult stem cells | | | | Gene therapy research | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | WR | U | Y | N | WR | U | Y | N | WR | U | Y | N | WR | U | Y | N | WR | U | Y | N | WR | U | Y | N | WR | U |
| Argentina* | X | | | | X | | | | X | | | | | X | | | | | X | X | | | | | | X | |
| Austria | X | | | | X | | | | X | | | | X | | | X | | | | X | | | | X | | | |
| Belgium | X | | | | | X | | | | X | | | | X | | | | | X | X | | | | | | | X |
| Brazil | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Bulgaria | X | | | | X | | | | | X | | | | X | | | | X | | | | X | | | | X | |
| Cameroon | X | | | | X | | | | X | | | | | | X | | | | X | | | | X | | | | X |
| Chile | X | | | | X | | | | X | | | | X | | | | X | | | X | | | | X | | | |
| China | | X | | | | X | | X | | | | X | | | | | | X | | | | X | | | | X | |
| Colombia | X | | | | X | | | X | | | | X | | | | | X | | | X | | | | X | | | |
| Croatia | X | | | | X | | | | | | X | | | | X | | | | X | | | | X | | | | X |
| Czech Republic | X | | | X | | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Democratic Republic of the Congo | X | | | | | X | | | | X | | | X | | | | | X | | | | X | | X | | | |
| Denmark* | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Dominican Republic | X | | | | X | | | | X | | | | X | | | | X | | | | | | X | | | | X |
| Egypt | X | | | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | |
| Finland | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | | | | X |
| France | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Greece | X | | | | | X | | | | X | | | | X | | | | X | | X | | | | X | | | |
| Hong Kong* | X | | | X | | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Hungary | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| India* | X | | | | X | | | | | X | | | | X | | | | X | | | | X | | | | X | |
| Ireland | X | | | | X | | | | | | X | | | | X | | | | X | X | | | | | | | X |
| Ireland (Republic) | X | | | | X | | | | | X | | | X | | | | X | | | X | | | | | | | X |
| Israel | X | | | X | | | | X | | | | X | | | | X | | | | X | | | | X | | | |

## Table 16.2 Research (continued)

### Is the following research possible in your country?

| Country | Reproductive cloning | | | Therapeutic cloning | | | | Research on embryonic stem cells | | | | Donate unused embryos for stem cell research | | | | Research on fetal stem cells | | | | Research on adult stem cells | | | | Gene therapy research | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Italy | X | | | | X | | | | | X | | | X | | | | | X | | | | X | | | | X | |
| Ivory Coast | X | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Japan | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Kazakhstan | X | | | X | | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Latvia* | X | | | | X | | | | X | | | | X | | | X | | | | X | | | | X | | | |
| Libya* | X | | | X | | | | | X | | | | X | | | | X | | | | | X | | | | X | | |
| Mexico | X | | | | X | | | X | | | | | | | X | | | | X | X | | | | X | | | |
| New Zealand | X | | | | X | | | | X | | | | X | | | | X | | | | | X | | | | X | | |
| Norway | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Peru | | | X | | | | X | | | | X | | | | X | | | | X | | | | X | | | | X |
| Philippines | X | | | | X | | | | X | | | | | | X | X | | | | X | | | | | | | X |
| Russia* | X | | | | X | | | | X | | | | X | | | | | X | | | | X | | | | X | |
| Saudi Arabia | X | | | | X | | | | | X | | | | X | | X | | | | X | | | | X | | | |
| Senegal | X | | | | X | | | | X | | | | X | | | | X | | | | | X | | | | X | | |
| Singapore | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | | X | | |
| Slovenia | X | | | | | X | | | | X | | | X | | | | X | | | | | | X | | | X | | |
| South Africa | X | | | X | | | | X | | | | X | | | | X | | | | X | | | | | | | X |
| South Korea | X | | | | | X | | | | X | | | | X | | | | X | | | | | X | | | | X | |
| Spain* | X | | | | X | | | X | | | | X | | | | | | | X | | | | | X | | X | |
| Sweden | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Switzerland | X | | | | X | | | | | X | | | | X | | | | X | | | | | X | | | | X | |
| Taiwan | X | | | | X | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Togo | X | | | | X | | | | | X | | | | X | | | | X | | | | | X | | | | X | |
| Tunisia | X | | | X | | | | | X | | | | | | X | | X | | | | | | | X | | | | X |
| Turkey | X | | | | X | | | | X | | | | X | | | | X | | | | | | | X | | | | X |
| Uganda | X | | | | X | | | | X | | | | X | | | | X | | | X | | | | | X | | | |
| United Kingdom* | X | | | X | | | | X | | | | X | | | | X | | | | X | | | | | X | | | |
| Uruguay | X | | | | X | | | | X | | | | X | | | | | | X | X | | | | | | | | X |

| Table 16.2 Research (continued) | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Is the following research possible in your country?** | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Country** | **Reproductive cloning** | | | **Therapeutic cloning** | | | | **Research on embryonic stem cells** | | | | **Donate unused embryos for stem cell research** | | | | **Research on fetal stem cells** | | | | **Research on adult stem cells** | | | | **Gene therapy research** | | | |
| United States | X | | | X | | | | X | | | | X | | | | X | | | | X | | | | X | | | |
| Venezuela | X | | | | X | | | | X | | | | X | | | | X | | | | X | | | | X | | |
| Vietnam | | | X | | | | X | | X | | | | | X | | | | X | | | | X | | | | X | |

**Y: Yes** **N: No** **WR: With restrictions** **U: Unknown**

* Multiple replies submitted for the country but only one response included in table.

# Chapter 17: Cloning

## INTRODUCTION

Reproductive cloning is a process in which an animal with the nuclear DNA of another animal is generated. The technique, called somatic cell nuclear transfer (SCNT), produces an almost identical twin that differs from an identical twin in that it has the mitochondrial DNA of the recipient egg. The prototype, the sheep named Dolly, was a product of such reproductive cloning. Reproductive cloning is extremely inefficient. The number of transferred cells that subsequently develop to live birth is approximately 1%-2%. There is a high incidence of abnormalities among the developed animals. This observation and pervasive ethical concerns preclude its application to clinical practice (1,2).

Therapeutic cloning is a process in which stem cells are harvested from the inner cell mass of human blastocysts. Stem cells may be perpetuated *in vitro* with the intent of having them undergo controlled differentiation for therapeutic purposes. Stem cells can be created by SCNT from a particular person or animal and offer the compelling advantage of avoiding transplant rejection since the cells or tissue are created from the same organism (1,2). This survey did not address stem cell technology.

## ANALYSIS OF THE SURVEY

***Reproductive cloning:*** Reproductive cloning was reported by the respondents to not be allowed in 45 of the 46 countries with formal statutes, laws, and guidelines. It is allowed in 1 (China with restrictions) of the 46 countries. Laws, regulations, statutes, or guidelines in virtually all countries prohibit use of reproductive cloning and none of the respondents report practicing it.

***Therapeutic cloning:*** Therapeutic cloning was reported by the repondents to be used in 8 of the 46 countries with formal statutes, laws, and guidelines. It is reported that therapeutic cloning is not used in 38 of the 46 countries. Laws, regulations, statutes, or guidelines in virtually all countries where it is officially allowed are reported as restricting use of therapeutic cloning to research. Research on embryonic stem cells is reported to be allowed in 14 of the 46 countries with formal statutes, laws, and guidelines; however, respondents from 28 out of the 46 countries reported donation of unused embryos for stem cell research (Table 17.1).

## DISCUSSION

Reproductive cloning, despite success in experimental animals and well-publicized initiatives with humans, has not produced a verified human birth. As reflected in this survey, reproductive cloning is reported as being prohibited in all but one country (China). Respondents state that there are no reports of it being attempted in China.

Therapeutic cloning, in which human IVF blastocyst serves as a source of human stem cells, is permitted in fewer than 20% of countries, from where respondents replied to these questions. In these countries, it is reportedly practiced under approved stem cell research initiatives.

## SUMMARY

Reproductive cloning is almost uniformly rejected as reported by respondents from countries who responded to these survey questions.

Respondents have stated that therapeutic cloning, with significant potential clinical therapeutic benefits, is

practiced under restriction in a limited number of countries.

## REFERENCES


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2. Trounson AO. Future and applications of cloning. Methods Mol Biol. 2006;348:319-32.

| Table 17.1 Therapeutic cloning | | | | |
|---|---|---|---|---|
| **Country** | **Used** | **Not used** | **Unknown** | **Comments from respondents** |
| Argentina* | | + | | |
| Australia | | + | | |
| Austria | | + | | See other section |
| Belgium | + | | | |
| Brazil | | + | | |
| Bulgaria | | + | | |
| Cameroon | | + | | |
| Chile | | + | | |
| China | | + | | |
| Colombia | | + | | |
| Croatia | | + | | |
| Czech Republic | + | | | Research usage |
| Democratic Republic of the Congo | | + | | |
| Denmark* | | + | | |
| Dominican Republic | | | + | |
| Egypt | | + | | |
| Finland | | + | | |
| France | | + | | |
| Greece | | | + | |
| Hong Kong* | | + | | |
| Hungary | | + | | |
| India* | | + | | |
| Ireland* | | + | | |
| Israel | + | | | |
| Italy | | + | | |
| Ivory Coast | | + | | |
| Japan | | + | | |
| Kazakhstan | | + | | |
| Latvia* | | + | | |
| Libya* | | + | | Not used yet |
| Mexico | | + | | |
| New Zealand | | + | | |
| Norway | | + | | |
| Peru | | + | | |
| Philippines | | | + | |
| Russia | | + | | |
| Russian Federation | | | + | |
| Saudi Arabia | | + | | |
| Senegal | | + | | |
| Singapore | | + | | |

| Table 17.1 Therapeutic cloning (continued) | | | | |
|---|---|---|---|---|
| **Country** | **Used** | **Not used** | **Unknown** | **Comments from resondents** |
| Slovenia | | + | | Prohibited |
| South Africa | | + | | It is allowed by law with permission from the Minister of Health, but not yet done in reality |
| South Korea | + | | | Only for research on rare or incurable diseases designated by the Presidential Decree |
| Spain* | | + | | |
| Sweden | | + | | |
| Switzerland | | + | | |
| Taiwan | | + | | |
| Togo | | + | | |
| Tunisia | | + | | |
| Turkey | | + | | |
| Uganda | | + | | |
| United Kingdom* | | + | | |
| Uruguay | | + | | |
| United States | + | | | There are some limitations and generally very limited federal funding for research in this area. |
| Venezuela | | + | | |
| Vietnam | | + | | |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 18: Status of the conceptus

## INTRODUCTION

The practice of ART in all countries in which it is performed is ultimately dependent on the perspective that each nation offers regarding the status of the conceptus. Practices are governed by moral and ethical values, guidelines and statutes, and the individual interpretation of these pronouncements. While the practice of medicine in general is governed by universally accepted ethical principles such as autonomy, justice, beneficence, and non-maleficence, their application to the practice of IVF poses unique challenges in their interpretation since there are inherent potential conflicts of interest between the prospective parents and their concepti. There is an extraordinary amount of variation around the world in the way that these conflicts are framed and resolved.

The issue ultimately devolves to the determination of when, in the course of human development, a human being is considered to exist. Various countries have addressed the status of the embryo in various ways, governed by their cultural and religious traditions and interpretations of the relevant ethical principles. Although many entities have forcefully expressed viewpoints about this, there is no universally accepted answer based on biologic, religious, or ethical standards. There is a considerable variation as to when this point is defined in IVF, and respondents to the current survey noted a range from the moment of fertilization to the time of birth (Table 18.1). Of countries that have favored a definition occurring in the course of development, 14 days has been commonly applied. This is an arbitrary definition that was initially suggested by the United States Ethics Advisory Board in 1978 but does correspond to significant embryologic events, including the development of the spinal column, which serve to establish biological individuation.

## ANALYSIS OF THE SURVEY

The 2013 Surveillance has noted relatively little change among countries in their outlook on this issue. However, several relevant events have occurred in the past 3 years. In December 2012, the Inter-American Court of Human Rights, based in San Jose, Costa Rica, over-ruled the Costa Rica Constitutional Chamber of the Supreme Court (Sala IV) 2000 decree that declared IVF unconstitutional on the grounds that it violated the constitutional guarantee to the embryo of the right to life (1). The Inter-American Court ordered Costa Rica to make IVF available within 1 year and to compensate the 18 victims who filed the suit for "violation of fundamental human rights." As of July 2013, no legislation to permit IVF has been enacted.

In the United States, the same issue has arisen in the form of several "personhood amendments" that have been proposed in at least nine states. These proposed laws are presented as bills or ballot initiatives and seek to confer legal rights and protection on the embryo at the moment of conception (2). Intended primarily to restrict access to abortion, the language of all of the personhood proposals potentially has extensive consequences for ART, including holding physicians legally liable for the fate of embryos not transferred and effectively curtailing IVF practices such as embryo cryopreservation. To date, none of the proposed legislation has been passed but several additional measures are currently being considered.

These efforts to redefine the point during gestation at which the US government has a vested role in protecting the unborn directly challenge the 1973 United States Supreme Court decision (Roe v. Wade) that guaranteed women the right to abortion in some circumstances. The initial ruling attempted to balance this right with two other concerns, protection of women's health and prenatal life. The initial ruling stated that access to abortion could be limited by trimester (unregulated during the first trimester, regulated to protect maternal health during the second trimester, and banned during the third trimester), but this framework was

subsequently modified by the Supreme Court in 1992 (Casey v. Planned Parenthood) to state only that the government could not unduly burden access to abortion up to the point of fetal viability, originally considered to be 28 weeks but now sometimes considered to be 24 weeks.

In the 2013 survey, respondents from 60 countries provided detailed information regarding whether there was a recognized time during human development that a human person was determined to exist and, if established, whether it was stipulated by statutes, guidelines, cultural practices, or recognized and prevailing religious decrees. Several respondents provided additional comments offering unique insights into their country's practices.

## REFERENCES


1. http://www.ticotimes.net/Opinion/Previous-editorials/In-Vitro-Fertilization-law-the-next-step
2. http://www.resolve.org/get-involved/personhood-bills-and-ballot-initiatives.html

| Table 18.1 Status of the conceptus | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? | | | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? How is this time determined? | | | | | |
| Country | Yes | No | Unknown | Law | Guidelines | Cultural practice | Recognized and prevailing religious decree | Unknown | Comments from the respondents |
| Argentina* | X | | | | X | | | | Conception is defined by SAMeR's guidelines as after implantation in the uterus has taken place |
| Australia | | | Null | | | | | Null | Null |
| Austria | | | X | | | | | Null | Null |
| Belarus | | | Null | | | | | Null | Null |
| Belgium | | X | | | | | | Null | Null |
| Brazil | | X | | | | | | Null | Null |
| Bulgaria | X | | | | X | | | | From the moment of birth, but pregnancy interruption is allowed up to 12 gestational week |
| Cameroon | | | X | | | | | Null | Null |
| Chile | X | | | | X | | | | Protection from conception |
| China | | X | | | | | | Null | Null |
| Colombia | | | X | | | | | Null | It is not mentioned |
| Croatia | | | X | | | | | Null | Null |
| Czech Republic | X | | | | X | | | | 12 weeks of pregnancy |
| Democratic Republic of the Congo | X | | | | | X | | | After fertilization, the embryo is considered as a human being |

| Table 18.1 Status of the conceptus (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? | | | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? How is this time determined? | | | | | |
| **Country** | **Yes** | **No** | **Unknown** | **Law** | **Guidelines** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| Denmark* | X | | | | X | | | | Week 20 |
| Dominican Republic | X | | | | X | | | | From the moment of conception |
| Ecuador | | | Null | | | | | Null | Null |
| Egypt | | | X | | | | | Null | Null |
| Finland | | | X | | | | | Null | Null |
| France | | X | | | | | | Null | Null |
| Greece | X | | | | X | | | | |
| Hong Kong* | X | | | | X | | | | Twelve weeks |
| Hungary | | X | | | | | | Null | Null |
| Iceland | | | Null | | | | | Null | Null |
| India* | X | | | | X | | | | 20 weeks |
| Ireland | X | | | | X | | | | After transfer to uterus |
| Ireland (Republic) | | X | | | | | | Null | Null |
| Israel | X | | | | | | X | | 40 days |
| Italy | X | | | | | X | | | Time of fertilization |
| Ivory coast | | X | | | | | | Null | Null |
| Japan | | X | | | | | | Null | Null |
| Kazakhstan | | X | | | | | | Null | Null |
| Latvia* | | X | | | | | | Null | Null |

| Table 18.1 Status of the conceptus (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? | | | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? How is this time determined? | | | | | |
| Country | Yes | No | Unknown | Law | Guidelines | Cultural practice | Recognized and prevailing religious decree | Unknown | Comments from the respondents |
| Libya* | X | | | | | | X | | 6 weeks |
| Mexico | | X | | | | | | Null | Null |
| New Zealand | | X | | | | | | Null | Null |
| Norway | | X | | | | | | Null | Null |
| Panama | | | Null | | | | | Null | Null |
| Peru | X | | | | | X | | | Since fecundation |
| Philippines | X | | | | | | X | | Fertilization |
| Portugal | | | Null | | | | | Null | Null |
| Russian Federation | | X | | | | | | Null | Null |
| Saudi Arabia | X | | | | | | X | | 6 weeks |
| Senegal | | X | | | | | | Null | Null |
| Singapore | X | | | | X | | | | 14 days |
| Slovenia | | X | | | | | | Null | Null |
| South Africa | X | | | | X | | | | 13 weeks as per the Choice of Termination of Pregnancy Act |
| South Korea | | X | | | | | | Null | Null |
| Spain* | | | X | | | | | Null | Null |
| Sweden | X | | | | X | | | | 23 weeks |
| Switzerland | | | X | | | | | Null | Null |
| Taiwan | | X | | | | | | Null | Null |
| Togo | X | | | | | X | | | 3 months |

| Table 18.1 Status of the conceptus (continued) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? | | | In your country, by statute/guideline/cultural practice/or recognized and prevailing religious decree, is there a recognized time during human development after which a human person is considered to exist? How is this time determined? | | | | | |
| **Country** | **Yes** | **No** | **Unknown** | **Law** | **Guidelines** | **Cultural practice** | **Recognized and prevailing religious decree** | **Unknown** | **Comments from the respondents** |
| Tunisia | | X | | | | | | Null | Null |
| Turkey | | X | | | | | | Null | Null |
| Uganda | X | | | | | | X | | Controversial |
| United Kingdom* | | X | | | | | | Null | Null |
| Uruguay | | X | | | | | | Null | Null |
| United States | | X | | | | | | Null | Null |
| Venezuela | | X | | | | | | Null | Null |
| Vietnam | | | X | | | | | Null | Null |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 19: Sex selection

## INTRODUCTION

Sex selection is used either for social reasons, mostly to balance families, or to prevent transmission of sex-linked inherited genetic disorders.

Three different strategies were surveyed:

***Sperm sorting:*** Sperm sorting is performed by flow cytometry, an automated *in vitro* process that separates sperm into X- or Y-enriched semen for insemination (1).

***IVF with PGD:*** IVF is performed and embryos of the desired sex are selected for transfer by PGD. IVF with PGD is more precise than other methods, being successful for the desired sex in up to 99% of cases (2). Some clinics combine sperm sorting with IVF and PGD to obtain a larger number of embryos of the desired sex for transfer.

***Other methods:*** Other methods include intercourse timing, sperm separation on an albumin gradient column followed by traditional insemination, and selective termination of established pregnancy of the unwanted sex after sex identity is established (presumably by amniocentesis, chorionic villus sampling [CVS], or cell free DNA analysis) (3). The survey does not separately address these strategies but tabulates responses under the category "other methods."

## ANALYSIS OF THE SURVEY

This survey has found that sex selection is reported to be allowed in 9 of the 46 countries with statutes, laws, and guidelines. Those countries are: Belgium, Czech Republic, Greece, Hong Kong, Israel, Libya, Russia, Saudi Arabia, and the United States (Table 19.1). It is reported as not being mentioned in the statutes of 5 of these 46 countries. It is reported as not being allowed in 29 of the 46 countries with formal statutes, laws, and guidelines. There are an additional 5-12 countries with no formal statutes, laws, and guidelines that, therefore, have no policies on sex selection according to the respondents. Sex selection is reported as being practiced by IVF with PGD in 14 of the 46 countries and by insemination alone in 1 of the 46 countries (Philippines) and by both IVF with PGD and insemination in 2 of the 46 countries (Mexico and the United States) (Table 19.1). Insemination methods are not completely broken out in the survey except for sperm sorting, which received no positive responses. Sex selection by selective termination received no responses but "other methods" were acknowledged by respondents from 2 countries.

## DISCUSSION

Sperm sorting with insemination of X- or Y-enriched semen has reported success rates of 75% for boys and 85% for girls (1). Sperm sorting thus carries considerable risk of having a child of the non-chosen sex. Although available by license internationally, sperm sorting received a zero response in the survey. IVF with PGD is far more accurate because it involves PGD selection of the appropriate sex for embryo transfer. IVF with PGD is expensive and is therefore likely to be used only in more affluent countries. Sex selection by IVF with PGD, with insemination alone or with both methods, is allowed and practiced in 20 countries. From this survey, sex selection by IVF and PGD only is practiced in 16 of the countries, by insemination alone in 1 country, and by both techniques in 3 countries (Table 19.1). Among the 20 responses indicating knowledge of active sex selection services, there is an even distribution of Muslim and

Christian countries.

Sex selection is particularly contentious when practiced for social reasons rather than genetic indications (4). Enquiry was not made as to whether sex selection was allowed for family balancing, for prevention of serious sex-linked genetic conditions, or both. The motivation of couples seeking sex selection for non-medical reasons (4) and medical indications (4) has been reviewed, and an extensive debate persists in the literature regarding the ethical legitimacy of both applications.

## SUMMARY

This survey reveals that relatively few countries perform sex selection. From the respondents surveyed, sex selection by either sperm sorting techniques and/or embryo biopsy is reported as being allowed by statute in only 9 countries, not allowed in 29, and not mentioned by law in 5, but is reported as being practiced by 1 or both techniques in 20 countries.

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| Table 19.1 Sex selection | | | | | | | |
|---|---|---|---|---|---|---|---|
| Country | Is sex selection practiced? | | | Is sex selection used? | | | |
| | Yes | No | Unknown | By IVF | By insemination | Both | Unknown |
| Argentina* | X | | | X | | | |
| Australia | | X | | | | | |
| Austria | | X | | | | | X |
| Belgium | | | X | | | | X |
| Brazil | | X | | | | | X |
| Bulgaria | | X | | | | | X |
| Cameroon | | X | | | | | X |
| Chile | | X | | | | | |
| China | | X | | X | | | |
| Colombia | | X | | X | | | |
| Croatia | | X | | | | | X |
| Czech Republic | X | | | X | | | |
| Democratic Republic of the Congo | | X | | | | | X |
| Denmark* | | X | | | | | X |
| Dominican Republic | | | X | | | | X |
| Egypt | X | | | X | | | |
| Finland | | X | | | | | X |
| France | | X | | | | | X |
| Greece | X | | | X | | | |
| Hong Kong* | X | | | X | | | |
| Hungary | | X | | | | | X |
| India* | | X | | | | | X |
| Ireland | | X | | | | | X |
| Ireland (Republic) | | X | | | | | X |
| Israel | X | | | X | | | |
| Italy | | X | | | | | X |
| Ivory Coast | | X | | | | | X |
| Japan | | X | | | | | X |
| Kazakhstan | X | | | X | | | |
| Latvia* | | X | | | | | X |
| Libya* | X | | | X | | | |
| Mexico | X | | | | | X | |
| New Zealand | | X | | | | | X |
| Norway | | X | | | | | |
| Peru | | X | | | | | X |
| Philippines | | X | | | X | | |
| Russia * | X | | | X | | | |
| Saudi Arabia | X | | | X | | | |
| Senegal | | X | | | | | X |

| Table 19.1 Sex selection (continued) | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Country** | **Is sex selection practiced?** | | | **Is sex selection used?** | | | |
| | **Yes** | **No** | **Unknown** | **By IVF** | **By insemination** | **Both** | **Unknown** |
| Singapore | | X | | | | | X |
| Slovenia | | X | | X | | | |
| South Africa | | X | | | | | X |
| South Korea | | X | | | | | X |
| Spain* | | X | | X | | | |
| Sweden | | X | | | | | X |
| Switzerland | | X | | | | | X |
| Taiwan | | X | | | | | X |
| Togo | | X | | | | | X |
| Tunisia | | X | | | | | X |
| Turkey | | X | | | | | X |
| Uganda | | | X | | | | X |
| United Kingdom* | | X | | | | | X |
| Uruguay | | X | | | | | X |
| United States | X | | | | | X | |
| Venezuela | X | | | | | | X |
| Vietnam | | X | | | | | X |

* Multiple replies submitted for the country but only one response included in table.

# Chapter 20: Fertility preservation

## INTRODUCTION

Fertility preservation is a new category and, therefore, was not included in past IFFS surveys. Public awareness on the impact of malignant disease on reproductive health and new preservation options are expanding to meet an increasing expectation for fertility preservation services (1). This demand has been sparked by increases in the survival rates and increasing numbers of newly diagnosed cancer patients of reproductive age who expect to survive. In the United States, the most prominent initiative is the *Oncofertility Consortium*, which reports that 40,000 women of reproductive age face fertility loss from cancer treatment each year (2).

In response to the experience in the United States, there is an expectation of increasing international demand for fertility preservation, as this reproductive technology becomes better known (1,2).

The survey did not specifically query international initiatives in fertility preservation, but it did request information on the three major technologies that make fertility preservation possible: *oocyte cryopreservation, embryo cryopreservation,*and *ovarian/testicular tissue cryopreservation* (3-5).

## ANALYSIS OF THE SURVEY

### *Oocyte cryopreservation*

Respondents have reported that oocyte cryopreservation is allowed in 39 of the 46 countries with formal statutes, laws, and guidelines, and that it is not mentioned in the statutes of 4 of these 46 countries. It is not reported to be allowed in any of the 46 countries included in this survey. Laws, regulations, statutes, or guidelines in virtually all countries where it is officially allowed were reported to limit use of oocyte cryopreservation. Oocyte cryopreservation is reported to be practiced in 46 countries (see Table 6.1).

### *Embryo cryopreservation*

Respondents have reported that embryo cryopreservation is allowed in 35 of the 46 countries with statutes. It is reported to not be allowed in 1 of the 46 countries: Italy. Respondents report that there are limits to duration of storage in 23 of the 46 countries and no limits in 19 of the 46 countries. Furthermore, time limits to storage, when specified by specific circumstances, range from 3 to 10 years (see Tables 6.1and 6.3).

### *Ovarian/testicular tissue cryopreservation*

Respondents have reported that ovarian/testicular cryopreservation is allowed in 32 of the 46 countries with statutes, and that it is not mentioned in the statutes of 11 of these 46 countries. It is reported as not being allowed in any of the 46 countries. Ovarian or testicular cryopreservation is reported as being practiced as a clinical service in 38 of the 46 countries where it is generally offered as a method of fertility preservation for patients diagnosed with malignant disease (see Table 6.1).

### *Sperm cryopreservation*

This technology, presumed universally available, was not tabulated in the survey.

## DISCUSSION

Currently, IVF technology, combined with embryo or oocyte cryopreservation, is the best option for preserving fertility. This survey examined three technology paradigms commonly embodied into fertility preservation programs (3,4).

### *Oocyte cryopreservation*

Oocyte cryopreservation has become commercially viable over the past 3-5 years. Its major advantage is that the potential, future male partner does not need to be specified at the time of oocyte collection. Except for considerable concern about future birth rates and insurance coverage, oocyte cryopreservation, as reflected in survey statistics, is not innately controversial as a method of fertility preservation. Oocyte cryopreservation is reported as being allowed in all of countries tabulated, but laws, regulations, statutes, or guidelines in virtually all countries where it is officially allowed are reported to limit use of oocyte cryopreservation.

### *Embryo cryopreservation*

Embryo cryopreservation has been a viable method of fertility preservation for over 25 years. Its major disadvantage is that it requires fertilization by a specific male partner who needs to be specified at the time of oocyte retrieval. Embryo cryopreservation is reported as being allowed in all but one country with time limits for duration of storage specified in many of the countries for whom respondents were surveyed.

### *Ovarian/testicular cryopreservation*

Ovarian/testicular cryopreservation is an option that has emerged over the past 10 years. Reproductive tissue, ovary or testicular, is readily cryopreserved, as are other tissues such as bone marrow. The major problem is the considerable uncertainty about revitalization after thaw. Reimplantation of ovarian tissue has met with case report successes only and many failures (5). Methods of restoring oocyte viability by *in vitro* maturation of primordial oocytes have been successful in laboratory animals, but is not an established option for human participants. Despite these issues, ovarian or testicular cryopreservation is reported to be practiced as a clinical service in 38 of the 46 countries with statutes, laws, and guidelines, where it is generally reported to be offered as a method of fertility preservation for patients diagnosed with malignant disease.

## SUMMARY

Because Surveillance 2013 is the first time that fertility preservation has been listed as a category, there is no previous tabulation available for comparison. Continued increases in survival rates of cancer patients of reproductive age and increasing expectations of survival in these individuals is likely to fuel expanding international demand for fertility preservations that may likely be reflected in the next 3-year survey.

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# Chapter 21: Conclusions

Surveillance 2013 reflects the maturation of IVF as a clinical practice worldwide. The outcome of this survey suggests an incremental growth of the number of IVF clinics. Although there have been isolated episodes of resistance to providing access to IVF, such as in Costa Rica, overall there appears to be broader acceptance of the legitimacy and effectiveness of IVF and the associated assisted reproductive technologies. This is evidenced through this report which shows that ART is increasingly being permitted and practiced in all countries that were represented in this survey. Most of these countries have been reported to be experiencing an increase in accessible ART services, but survey respondents registered their concern that these services need to be provided in a safe and more equitable manner to address those who require ART. Increased surveillance of laboratories and stronger sanctions for violations were noted by this year's respondents, as was the observation that more clinics worldwide are further restricting the number of embryos transferred. Based upon the answers provided by the 2013 survey respondents, over the past 3 years, there appears to have been little change in the evolution of statutes or guidelines that address the welfare of the child.

The respondents have reported that IVF is generally practiced with broad social tolerance and this 2013 survey has exposed a trend towards greater inclusiveness and disclosure in dealing with issues such as anonymity with donor gametes. While there are significant differences reported from respondents in the approaches various countries take toward the application of donor gamete therapy, there appears to be wider consensus about more ethically contentious issues such as sex selection, which was reported to be practiced in a minority of the countries, as was similarly reported concerning the technique of reproductive cloning, which was almost universally prohibited. Furthermore, respondents confirmed, as previously reported by past surveys, that experimentation on the embryo continues to only be permitted in relatively few countries.

Respondents have reported an enthusiastic acceptance and utilization of newer innovative technologies for both infertile and subfertile patients, as well as non-infertile patients requiring these specialized services. Preimplantation genetic diagnosis was reported to be performed more commonly and there is renewed interest in preimplantation genetic screening. In addition, newer practices, such as *in vitro* maturation, and fertility preservation options for oncology patients, including sperm, oocyte, and embryo cryopreservation, are increasingly being introduced.